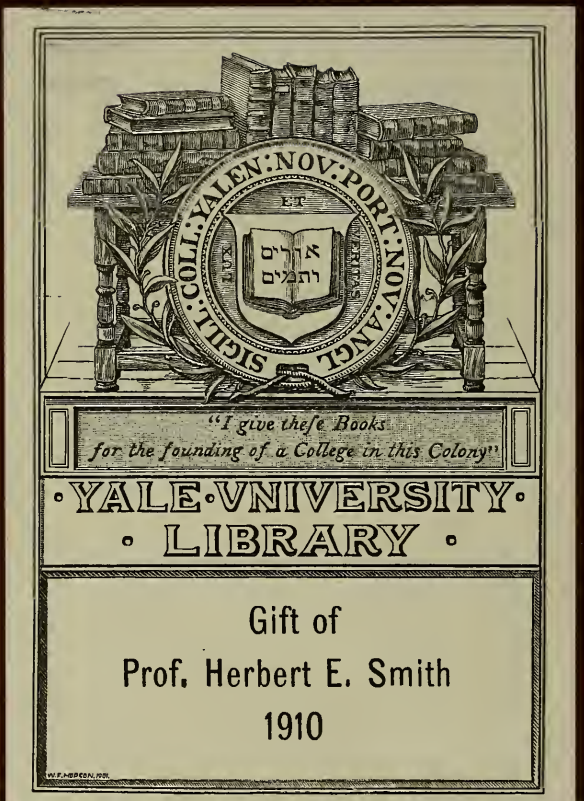
HELBING'S MODERN MATERIA MEDICA.



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MODERN MATERIA MEDICA

FOR

Medical Men, Pharmacists, and Students.

BY

H. HELBING, F.C.S.

FOURTH ENLARGED EDITION.

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INTRODUCTION TO FOURTH EDITION.

Two years have elapsed since the publication of the third edition of this MODERN MATERIA MEDICA, and during that time quite a large number of new synthetical remedies have been introduced into medicine, and the stock of information has been materially added to respecting those remedies already treated of in this book.

The advance of therapeutical science in these times is continuous as well as rapid. No breathing space is afforded the recorder of pharmacological progress. Thus after these pages had been finally read for press a new salt of antipyrine, the *mandelate* or *phenylglycolate*, under the name of *Tussol*, was recommended for whooping cough. According to Dr. Rehn it develops a more favorable action than antipyrine itself, both ameliorating the complex symptoms and diminishing the intensity of the convulsive attacks, whilst it can be administered to infants twelve months old in doses of 1 to 1½ grains twice or thrice daily, or in doses of 8 grains thrice or more daily to children four years of age and upwards.

Unfortunately a great number of preparations have been brought before the physician which are nothing more than palpable, and in some cases inferior, imitations of remedies already in existence, but which are reproduced with some slight and immaterial addition or alteration in order to gratify the passion for novelty, quite apart from the slightest consideration of advantage; yet these are also treated in this book to render it complete and up to date.

No effort has been spared to make the book as efficient an aid as possible, and to incorporate all trustworthy and useful information that has appeared in medical, pharmaceutical and chemical literature having reference to the special materia medica treated of in this volume.

The First Part of the book, which must be considered the principal and most important section, contains half again as much matter as in the previous edition, and about three times as much as in the second edition.

The Second Part of the book, which must clearly be understood from the introductory remarks on page 180 to be considered only of secondary importance, is in no way meant to include all those substances introduced into therapeutical use, which were not treated of in the first part. The Appendix is only intended to supplement to some extent the main portion of the book, and is not put forward as an exhaustive and complete treatise.

The tables at the end of the book have not only been brought up to date, but it has also been deemed advisible to add two further tables dealing respectively with special tests for a number of the newer remedies in the urine, and with the scientific nomenclature of the commercial names adopted. The table of chemical tests will, it is hoped, prove useful not only in facilitating the detection of these drugs in urine analysis, but also in explaining abnormal appearances or behavior in the application of clinical tests. In the multiplication and confusing similarity of commercial names the second table will also no doubt be frequently found handy for reference.

Thus in placing the fourth edition of Modern Materia Medica before the professions, it is hoped that it may find the same friendly reception as previous editions, and be not only of practical use, but also aid those who wish to acquire a concise idea of the composition of new remedies, and of their physical and chemical characteristics.

London : September, 1894.

INTRODUCTION TO THIRD EDITION.

During a period of twelve months no branch of science in this age stands still. New experiments are constantly being devised and carried out, old ones are repeated; innumerable new facts are brought to light and relationships hitherto unsuspected or only guessed at are established between those already ascertained; everywhere the spirit of investigation, the spirit of inquiry is at work.

Perhaps nowhere is this restless progressive tendency more conspicuous than in pharmacology, and especially in that of the synthetical class of remedies which forms the principal subject of this work. It is true that the study of all the remedies has not been advanced to the same degree and that a few seem to have been even entirely neglected, but with these rare exceptions, the literature—chemical in a number of cases, pharmacological in a great many—of the substances treated in the preceding edition has developed and increased to a marked extent.

These additions not only constitute fresh material to be included in a revised edition of Modern Materia Medica, but in a large number of cases have an effect upon the balance of opinion which has been expressed upon the value of certain of the substances treated.

For this reason it has been found necessary to entirely rewrite those parts which summarise the therapeutical uses of the compounds, while in a considerable proportion of cases the same has been made necessary in the other divisions of the monographs by the publication of recent researches on the chemistry of the synthetical remedies.

This revision and extension of the subjects of the preceding edition and the inclusion of a number of entirely new additions to the class of substances treated have made it necessary to add about forty pages to—that is to increase by half as much again—the first part of the book.

Some of the new-comers have been considered to be of sufficient importance to require description in separate monographs, but a greater number has been added as "Derivatives and Allied compounds" to the chapters which appeared in the previous edition.

Even in the few weeks that have elapsed since these pages were closed for press papers have appeared on new substances which are being brought under the notice of medical men. Diaphtherin (oxychinaseptol) (OH. $C_9H_6N)_2$ (OH) (SO_3H) C_6H_4, and Asaprol (calcium–β–naphtol–α–monosulphonate) (OH. C_{10} H_6 $SO_3)_2$ Ca, 3 Aq., are antiseptics comparatively non-poisonous and soluble in water; the former is a powder which in 0.1 per cent. solution kills the cholera bacillus in 10 minutes, while the latter occurs in acicular crystals and in 5 per cent. solution prevents the growth of the most resistant bacilli.

The purpose and scope of the Appendix are sufficiently explained in the introductory words which immediately precede it. It has been very largely increased in bulk and includes a class of compounds (vegetable in origin) which, with a few exceptions, were not given a place in the second edition.

Special care has been taken with the terminology adopted in order to make it accord, so far as possible, with the rules which have been laid down by the best authorities for the guidance of English writers on chemical subjects.

London: May, 1892.

INTRODUCTION TO SECOND EDITION.

Synthetical remedies have become one of the distinctive features of our time. The zeal and untiring energy of the old alchemists in their search for the philosopher's stone and the elixir of life are reproduced to-day in the eager quest of their scientific descendants for artificial alkaloids.

Since the time when the modern chemist first became fired with the ambition to win fame and wealth at one stroke by the synthesis of quinine, the number of remedies turned out yearly from the chemical laboratory has gone on steadily increasing, and if the original aim of the work is still unaccomplished—as the process of M. M. Grimmaux and Arnaud is but a partial solution of the problem—yet among the very considerable number of compounds produced, some have been found capable of replacing the natural alkaloid in many cases, while in others they seem to be even superior to it in therapeutical activity, reliability or safety.

Not a few of the medical agents, thus, as it were, created, have won the favour of the medical profession sufficiently to secure them a place in the chief European Pharmacopœias. But there is a much larger number, the members of which are still on trial—passing through their period of probation—and of these, of course, there is no official recognition. Nevertheless their importance is, in some instances, not at all inferior to that of the pharmacopœial compounds, and hence they are more or less generally used by the medical man, and cannot be ignored by the pharmacist who desires to keep abreast of the times.

Naturally, however, the literature of substances produced at different times by various manufacturers and examined by pharmacologists and chemists in all parts of Europe and of the civilized world is widely scattered, and not easy to come at. For this and other more or less potent reasons it has become exceedingly difficult, if not impossible, for the busy medical man or pharmacist to maintain his acquaintance with the properties and uses of therapeutical novelties continually being brought under his notice in the scientific press of the country.

To be *au courant* with the growth of synthetical materia medica, however desirable, is, however, not all that the followers of medicine and pharmacy require. Information of this kind, if it is to be of practical service, must be in such a form as to be available for ready and more or less frequent reference.

It is the aim of the following pages to supply the want generally felt in this country of full and comprehensive details as to the constitution, methods of preparation, tests and medicinal application of new remedies. The requirements not only of the pharmacist, but also of the therapeutist and general practitioner, have been kept in mind; while further, the work is designed to rank as a text book for purposes of study. It would, perhaps, be well to add that in dealing with "medical uses" of each compound, it has been a constant endeavour to indicate its therapeutical importance, where possible, rather by a careful balancing of the whole literature of the subject than by a detailed quotation of individual experiences and quotations.

Every monograph has been carefully revised and extended, where necessary, in order to make the volume representative of the progress of synthetical remedies down to the date of issue. It is believed, that the practical value of the work to all classes of readers will be enhanced by the appendix, the various tables, and not less by the index, with which equal care has been taken.

London: June, 1891.

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MODERN MATERIA MEDICA.

ACETANILIDE.

Synonyms : ANTIFEBRINE ; PHENYLACETAMIDE.

$C_6H_5NH.CH_3CO.$

One of the most simple synthetical compounds of the "new remedy" era. Is now official in the British and United States Pharmacopœias under the name "Acetanilidum."

Preparation.—By the prolonged interaction of pure aniline (boiling point 184° to 185° C.) and glacial acetic acid at a high temperature. Fractional distillation—collecting what passes over at 295° C.—and recrystallization from boiling water. The reaction may be thus represented :—

$$\underset{\text{Aniline}}{C_6H_5NH_2} + \underset{\text{Acetic acid}}{CH_3COOH} = \underset{\text{Acetanilide}}{C_6H_5NH.CH_3CO} + H_2O.$$

It should be observed that simple as this process appears on paper, it is practically very difficult to obtain a pure product even with special plant and large experience.

Physical and Chemical Properties.—When pure, acetanilide forms lustrous rhombic tables without color or odor, but with a peculiar greasy feel and a slight burning taste. It requires nearly 200 parts of water at 15° C. for solution, but only 18 of the same solvent at 100° C. (forming neutral solutions); soluble in alcohol (1 : 3½), readily in ether and in chloroform. According to the B. P. Addendum the crystals should melt at 112.8° C. (235° F.); according to the U. S. P. at 113° C.; by Ritsert the melting point of pure acetanilide is said to be 114° C.; it is evidently above rather than below 113° C. When melted acetanilide forms a clear colorless liquid which distils unaltered at 295° C. By continued contact with hydrochloric acid or potash at high temperatures it splits up into its components.

Acetanilide is identified in the additions to the B. P. 1885 by the development of the odor of phenyl-isonitrile when heated with solution of potash and a few drops of chloroform, but this test is not sufficient for the identification of acetanilide, as other synthetic products of similar constitution, like phenacetine, afford the same reaction, though less readily.

Other characteristic reactions are the formation of the yellow coloring substance with a beautiful moss-green fluorescence (flavaniline, $C_{16}H_{14}N_2$) when heated for some time with an equal weight of zinc chloride. Six grains boiled for a few minutes with 1 fl. drm. of hydrochloric acid form a clear solution, which, on the addition of 3 fl. drms. of water and 4 drops of carbolic acid previously dissolved in ½ fl. drm. of solution of chlorinated lime, assumes a turbid, dirty-red color, and, on the further addition of excess of ammonia, an indigo-blue (indophenol). A drop of 1 per cent. chloride of lime solution on a glass rod, held at the mouth of a test tube in which a few grains of acetanilide are boiled with caustic potash solution, turns yellow with violet tinge, and finally violet (Vulpius).

Free acetic acid is detected by the litmus reaction, acetone by ferric chloride, which must not affect the *cool*, aqueous solution, and aniline by solution of 15 grains in 1 fl. oz. of hot water (the solution is turbid if aniline be present, and smells of the latter). General impurities are detected by determination of the melting point and ignition on platinum foil (no residue should be left).

Ritsert states that a boiling solution of 15 grains in 1 fl. oz. of water is colored rose-red by one drop of a 0.1 per cent. aqueous solution of potassium permanganate, and that this color persists for at least five minutes.

Means of distinction from phenacetine, methacetine and exalgine are given under **Exalgine** (*q. v.*). Detection of acetanilide and its derivatives in urine is best effected by the indophenol reaction (v. supra), or by extracting the urine with chloroform and heating the chloroform residue in a procelain dish with mercurous nitrate; a green colored mass, soluble in alcohol with green color, is obtained if present (Yvon).

Medicinal Uses.—Under the copy-righted name "antifebrine," acetanilide was introduced into medicine as an antipyretic in 1887. Its use in combatting the febrile temperature of acute rheumatism emphasized its analgesic virtues, and its principle employment has been in the treatment of neuralgias and rheumatism. As an antipyretic, in phthisis and other pulmonary affections, in typhus and fevers generally, it has been largely replaced by remedies of more recent date; but it has been recommended within the last few months in the treatment of acute bronchitis (4 grains every two hours), the attacks being often arrested within 24 hours (Gruen). It has been credited with valuable properties in improving weak and irregular pains in labor.

There is considerable literature relative to the serious by- and after-effects which sometimes accompany or follow the remedial action of acetanilide. Though it is not improbable that these unpleasant experiences may have been in some cases due to impurity of the specimen used, yet it does appear that its employment requires watchful care.

The substance is not to be recommended for external application as an antiseptic.

The powerful physiological effects of acetanilide make it necessary to keep a watch upon its possible admixture, fraudulently or accidentally, with other synthetical antipyretics of which considerably larger doses are given.

The average dose of acetanilide is between 3 and 8 grains, in powder, or wafers, capsules, etc. In certain conditions, *e. g.* in typhus, it is recommended to begin with quite small doses (1½ grains).

A purely pharmaceutical use of acetanilide has recently been suggested; its addition in small proportion to aqueous hypodermic solutions is said to preserve them from decomposition better than any other agent hitherto employed for the same purpose (Keenan).

DERIVATIVES AND ALLIED COMPOUNDS.

Many derivatives and compounds analogous to acetanilide have been prepared, a few of which have found therapeutical application, but many of which are devoid of antipyretic properties or possess toxic qualities.

Mono- or Para-Brom-Acetanilide, also termed *Asepsine* or *Antisepsine*, $C_6H_4BrNH.CH_3CO$, forms colorless monoclinic prisms, melting at 165° to 166° C., fairly soluble in alcohol, practically insoluble in water. Recommended as anodyne and analgesic in doses of 1½ grains in neuralgia; also as an antiseptic. Its literature is very scanty. The name *Antisepsine* has unfortunately also been recently given to a serum lymph obtained by injecting iodine trichloride solution into abscesses.

Para-Iod-Acetanilide, $C_6H_4INH.CH_3CO$, melting at 181.5° C., fairly soluble in hot water, easily soluble in alcohol, has not come into use in medicine, as it passes the organism undecomposed and is devoid of antipyretic properties.

Diacetanilide, $C_6H_5N(CH_3CO)_2$, is identical in therapeutical action to ordinary acetanilide (Hildebrandt).

Bromamide, or tribromaniline hydrobromide, $C_6H_2Br_3.NH_2.HBr$, occurs in colorless, tasteless crystals, melting at 117° C., insoluble in water, slightly soluble in alcohol, and is brought into the American market as an excellent neuralgic. Administered in doses of 10 grains several times daily (Caillé).

Other derivatives of aniline will be found under **Benzanilide** and **Exalgine.**

Salicyl-bromanilid, *Salbromalid*, and *Antinervin*, are the names under which a substance was brought under the notice of medical men early in 1890, and described as a combination of bromacetanilide and salicylanilide. According to an exhaustive examination by Ritsert, antinervin is a mixture of ammonium bromide, salicylic acid and acetanilide (1 : 1 : 2), and, therefore, cannot be administered with safety in quantities which contain more than the average dose of acetanilide.

Antikamnia. This name was given by an American firm to a preparation introduced as a substitute for morphine, and as an antipyretic and analgesic. It was manufactured as a fine white powder, which gave evidence of its non-homogeneity when examined under the microscope. Several analyses of "antikamnia" were published which all agreed in finding the chief constituents to be acetanilide with bicarbonate of soda. The proportions of these components seem from the

analyses to have varied, and some observers detected caffeine, tartaric acid and other additions.

Phenolid was brought out as a competitor of "antikamnia." According to an analysis, published in America, it is a mixture of acetanilide and salicylate of soda, in the respective proportions of 58:43. Similar preparations have still more recently appeared from the New World, as

Exodyne (ἐξ and ὀδύνη, pain), a white powder, in which the microscope plainly reveals bodies of different crystalline form. Its average composition proved (Goldmann) to be acetanilide (90 per cent.), sodium salicylate (5 per cent.), and sodium bicarbonate (5 per cent.).

Antikol, a powder consisting of acetanilide (75 per cent.), sodium bicarbonate (17.5 per cent.), and tartaric acid (7.5 per cent) [Goldmann], is practically only an effervescent acetanilide.

Pyretin is a mixture of acetanilide, caffeine, carbonate of lime and bicarbonate of sodium, practically identical with antikamnia (Welter).

Phenatol is a similar mixture of acetanilide, sodium bicarbonate, sodium carbonate, sodium sulphate, sodium chloride, and caffeine succinate in varying proportions (Welter).

Kaputin consists of colored acetanilide.

AGATHIN.

Synonym: SALICYL-α-METHYLPHENYLHYDRAZONE.

$$C_6H_5 . N(CH_3) . N : CH . C_6H_4(OH).$$

A compound of salicylic aldehyde with the base methylphenylhydrazine, belonging to the class of "hydrazones," and first prepared by J. Roos in 1892.

Preparation.—By the interaction of molecular equivalents of asymmetrical methylphenylhydrazine and salicylic aldehyde at ordinary temperatures, either direct or in solution in methyl or ethyl alcohol. The product is recrystallized from hot alcohol.

Physical and Chemical Properties.—Agathin forms white or greenish-white crystalline leaflets, insoluble in water, soluble in alcohol, ether, benzene and ligroin. Its melting point is 74° C.

Shaken with water the filtrate is not discolored by ferric chloride, or on addition of dilute sulphuric or hydrochloric acids. It is decomposed by warming with hydrochloric acid. Dissolved in concentrated sulphuric acid a brownish-yellow colored solution is produced, which on addition of a trace of concentrated nitric acid changes to blue and finally to green.

The cold saturated aqueous solution is not altered in the cold or warm by silver nitrate. Heated on platinum foil the crystals burn without residue.

Medicinal Uses.—As an antineuralgic and antirheumatic. Agathin has been successfully employed in articular rheumatism, sciatica and neuralgias in cases where sodium salicylate and other remedies have proved ineffectual (Ebeling, Rosenbaum, Schmidt, Laquer and Löwenthal).

Its anodyne properties are not always immediately displayed, but generally only after two or three days' administration. The adult dose adopted is 8 grains, three times a day, as powder, or given in lemonade if nausea is present. After three or four days the daily dose is reduced to 16 or 8 grains.

In general experience agathin possesses a very mild action, and is free from unpleasant by- or after-effects, though the great energy of most simpler phenylhydrazine derivatives demands caution, and has led to untoward symptoms in a few instances (Gerhard and Bad).

ALLIED COMPOUND.

Malakin, or *Salicylphenetidine*, $C_6H_4(OC_2H_5).N:CH.C_6H_4(OH)$, is a compound of salicylic aldehyde with the base paraphenetidine. It is not to be confounded with **Saliphen** (*q. v.*), which is a compound of the same base with salicylic acid. Malakin occurs in small bright yellow needles, melting at 92° C., insoluble in water, difficultly soluble in cold, and easily in hot alcohol. Dilute mineral acids split it up into its components. Dissolves in caustic alkalies. Employed as agathin in acute rheumatic affections in 15 grain doses up to 60 or 90

grains *pro die.* It possesses a slow and mild antipyretic action, and is an excellent analgesic in neuralgias, free from by-effects (Jaquet, Immermann). Indicated in the fever of consumptives in consequence of its mild action, and as an anodyne free from bad effects (Bauer).

ALUMNOL.

Synonym: β-Naphtoldisulphonate of Aluminium.

$(C_{10}H_5(OH)(SO_3)_2)_3Al_2$.

The contracted name of an organic aluminium salt introduced into therapeutical employment by Heinz and Liebrecht in 1892.

Preparation.—By heating together β-naphtol with three parts of concentrated sulphuric acid at 110° C. β-naphtoldisulphuric acid is produced, which is converted into the barium salt, and ultimately by decomposition with the theoretical quantity of aluminium sulphate into the aluminium salt.

Physical and Chemical Properties.—A colorless non-hygroscopic powder, which dissolves easily in cold water and in glycerin, slightly in alcohol, and is insoluble in ether. The aqueous solution, which can be prepared up to 40 per cent. strength by the use of hot water, is slightly acid in reaction, like that of all aluminium salts, and is colored blue with ferric chloride. Both aqueous and alcoholic solutions exhibit a blue fluorescence.

Aqueous solutions of alumnol give a white gelatinous precipitate of aluminium hydrate with ammonia, insoluble in excess, soluble in caustic soda.

Alumnol precipitates albuminoid and gelatinous bodies from solution, but the precipitate redissolves in excess of albumen or gelatine. It darkens on exposure to air in consequence of its reducing properties.

Medicinal Uses.—As an antiseptic and astringent, which in consequence of its peculiar behavior toward albumen, etc., has a superior penetrating action into the tissues to other

salts of heavy metals, as silver nitrate, and is preferable to aluminium acetate.

The astringent action of alumnol is distinguishable by the tongue in 0.01 per cent. solutions, and on the mesenteries of the frog in 0.0025 per cent. solution. Irritant action first appears with 5 per cent. solutions and corrosive action with 10 per cent. Its antiseptic action is also apparent in 0.01 per cent. solution, retarding the development of gonococci and pus cocci and other bacteria, and in 0.4 per cent. solutions prevents all growth.

Purulent surfaces and cavities are readily cleansed by 1 or 2 per cent. solutions, and weak ulcers favorably treated with 3 to 6 per cent. ointments. A 10 to 20 per cent. solution serves as a cautery in small abscesses and fistular openings. In gynæcology the penetrating action of 1 to 2 per cent. alumnol solution is specially serviceable in endometritis gonorrhoica (Asch, Chotzen). In otitis media purulenta it is employed as a powder or solution (Brieger), the solubility of alumnol in purulent secretions preventing the stoppage of channels and vessels discharging pus. The 4 per cent. solution is useful for cleansing the eyes in blennorrhœa (Wolffberg). In skin affections, both in superficial inflammation and in chronic infiltrated conditions, alumnol plasters, plaster mull, and varnishes are conveniently employed (Chotzen). Besides the principal use of alumnol in gonorrhœa, the ¼ to 1 per cent. solution has found extensive employment as a gargle in inflammation of the mouth, pharyngeal and laryngeal mucous membrane.

ALLIED COMPOUNDS.

Sozal, or *para-phenolsulphonate of aluminium*, $[C_6H_4(OH)SO_3]_3Al$, is a similar preparation bacteriologically and clinically examined by Girard and Lüscher. Prepared from phenol in an analogous manner to alumnol, it is a crystalline powder with astringent taste and slight phenol odor, resembling alumnol in physical and chemical properties. Its aqueous solution, which is colored violet by ferric chloride, precipitates albumen but the precipitate is soluble in excess of albumen. Employed in 1 per cent. solution in purulent affections, tuberculous ulcers and cystitis (Lüscher).

Salumin, or *aluminium salicylate*, is a reddish-white powder, insoluble in water, employed as a dusting powder in catarrhal affections of the nose and pharynx, especially in ozæna (Heymann). A soluble salumin is also prepared by treatment with ammonia, and employed with like indications.

Gallal, a basic *gallate of aluminium*, formed by precipitation of an alumina solution with sodium gallate, is a brown, amorphous, insoluble powder, recommended as a disinfectant in ozæna simplex. The double ammonium salt crystallizes in lamellæ, is stable, and soluble in water.

Tannal, a basic *tannate of aluminium*, prepared in an analogous manner, is a brownish-yellow insoluble powder, employed as astringent in chronic catarrh of the respiratory organs. A soluble tannal is prepared by treatment of the insoluble form with tartaric acid, and employed with like indications.

Argentamine, or *Ethylenediamine-Silver Phosphate*, a solution of silver phosphate in ethylenediamine, is an organic preparation intended to secure the penetration of silver salts into deep-seated tissues. Argentamine is a colorless, clear liquid, containing twice as much ethylenediamine as silver phosphate, and with an alkaline reaction dependent upon the amount of ethylenediamine present. The 10 per cent. solution contains as much silver as a 10 per cent. solution of silver nitrate. Like all silver salts the preparation must be preserved in the dark as it is extremely susceptible to light. The organic silver phosphate solution gives no precipitate with albumen or serous fluids, owing to the solvent character of ethylenediamine, which is an organic base, $C_2H_4(NH_2)_2$, forming a clear, colorless liquid of ammoniacal odor, easily soluble in water, and without toxic or corrosive properties.

Owing to the penetrating action and high bactericidal qualities of argentamine, and being non-irritating, it is specially indicated in gonnorrhœa (Neisser, Schaeffer). Its toxicity is not greater and its germicidal powers are far higher than those of silver nitrate solution of equal percentage of silver.

AMYLENE HYDRATE.

Synonyms: Dimethylethylcarbinol; Tertiary Amyl Alcohol.

$(CH_3)_2C_2H_5COH$.

One of the eight possible alcohols, with the general formula $C_5H_{12}O$. First prepared by Wurtz, and identified later by Flavytzky and Osipoff.

Preparation.—By the action of sulphuric acid upon amylene at a low temperature, separation of the amylenesulphuric acid, dilution with ice-cold water, filtration, neutralisation (with chalk or soda) and distillation. The distillate is freed from water by potash and fractionated, the fraction which passes over between 100° and 102.5° C. being collected.

Physical and Chemical Properties.—Amylene hydrate is a limpid, colorless, hygroscopic liquid, with a peculiar penetrating ethereal odor, which reminds of camphor and peppermint. Its specific gravity is 0.815, and when pure it boils at 102.5° C. In a mixture of salt and ice it solidifies at −12.5° C. to long acicular crystals, which melt at −12° C. Amylene hydrate dissolves in 8 parts of water at 15° C., the solution becoming turbid when warmed. It is miscible in all proportions with alcohol, ether and chloroform.

By oxydation with chromic acid it splits up into acetic acid and acetone.

Amylene hydrate is tested by determination of the physical factors. The liquid must not affect blue litmus (sulphuric acid) nor decolorize weak potassium permanganate solution within 15 minutes (ethyl or amyl alcohol). 15 minims dissolved in ½ fluid ounce of water, to which are added 10 drops of argentic nitrate solution and 1 drop of ammonia, should not give a mirror or precipitate metallic silver when warmed (aldehyde). As already stated the liquid is hygroscopic, and therefore control must be kept upon the presence of water by the boiling point (which it lowers); by agitation of 2 fl. drachms with 10 grains of exsiccated cupric sulphate no powerful blue color should be produced.

Medicinal Uses.—This tertiary amyl alcohol was first recommended by Professor von Mering, who regarded it as specially useful in cases of nervous sleeplessness, as it did

not manifest any action on the respiratory or circulatory systems. This lead was followed by other medical men (Avellis, Gürtler, Mayer, Rosenbach, Wildermuth), who ascribed anodyne as well as hypnotic properties to it. The adult dose adopted was 45 to 60 minims.

Two to five tablespoonful doses of a 10 per cent. aqueous solution have been effective in reducing the number of attacks in most forms of epilepsy (Naecke). When the patients have been previously taking bromide it would appear that considerable care is required, as in a number of cases of this kind the number of attacks increased and there was great restlessness. In a case which had resisted the action of all other remedies, amylene hydrate was also without effect (Drews).

In therapeutical activity amylene hydrate seems to be inferior to chloral, and it is not well borne when given for prolonged periods. It has proved successful in doses of 3 or 4 minims in the whooping cough of children.

Amylene hydrate is preferably given in solution (at least 8 parts of water being required), either aqueous or vinous, with raspberry syrup.

ANTHRAROBIN.

Synonyms: Desoxyalizarin ; Dioxyanthranol.

$$C_6H_4 \left\{ \begin{matrix} C(OH) \\ CH \end{matrix} \right\} C_6H_2(OH)_2.$$

A phenol derivative, allied to chrysophanic acid, and described as a leuco-substance.

Preparation.—By the reduction of commercial alizarin in warm ammoniacal solution with zinc dust, and filtration of the resultant solution into water acidulated with excess of hydrochloric acid. The precipitate is washed by decantation until free from acid, collected on clay plates, and dried at 100° C.

Physical and Chemical Properties.—Commercial anthrarobin is a yellowish-white powder, practically insoluble in water and dilute acids. Being a phenol derivative, it dissolves readily in the cold in dilute aqueous solutions of the alkalies and alkaline earths, these solutions being brownish-

yellow, and greedily absorbing oxygen (by which alizarin is re-formed). Anthrarobin is difficultly soluble in chloroform and benzene, but readily in 5 parts of alcohol; also soluble in glycerin.

Twenty-four grains should dissolve in ½ fl. oz. of soda solution to a clear solution, which assumes a violet color if air is passed through it (1 grain absorbs 120 to 130 grain measures of oxygen). Should not leave more than 1 to 2 per cent. of residue when burned on platinum foil.

Medicinal Uses.—As a substitute for chrysarobin in skin diseases (Behrend), especially psoriasis. On the one hand its non-staining and unirritating properties have been commended (Liebermann and Pick), but on the other it has been characterized as practically worthless (Rosenthal and Köbner). No fresh reports have appeared upon its use for some time, and it seems to have been forgotten.

ANALGENE.

Synonym: Ortho-ethoxy-ana-monobenzoylamido-chinoline.

$$C_9H_5(OC_2H_5)NH(COC_6H_5)N.$$

A chinoline derivative, corresponding to the phenacetine of the benzene series, prepared by Vis in 1892.

Preparation.—By introducing successively an ethyl and amido group into ortho-oxychinoline, in the same manner as in the preparation of phenetidine from phenol, and heating the resulting amido base with benzoyl chloride.

Physical and Chemical Properties.—White tasteless crystals of neutral reaction, insoluble in water, easily soluble in hot alcohol and also in dilute mineral acids. The crystals melt at 208° C., and leave no residue on incineration.

The cold saturated aqueous solution is colored only yellow by ferric chloride, citron-yellow by mineral acids, and does not reduce silver nitrate either in the warm or cold.

Medicinal Uses.—The preparation was recommended on account of its antifebrile and antineuralgic properties (Loebell). Employed successfully as a nervine in various neuralgias, cephalæa, migraine, trigeminus neuralgia, muscular rheum-

atism and gout, and against the sequelæ of tabes, alcoholismus and hysteria (Knust, Krulle, Treupel, Goliner, Spiegelberg). In doses of 8 grains 5 or 6 times daily. Administered best in powder form or in alcoholic solution. It appears to be free from bad effects, and has the advantage of freedom from taste. The urine is colored blood-red, changing to yellow on addition of alkali.

ANTIPYRINE.

Synonyms: Dimethylphenylpyrazolon; Dehydrodimethylphenylpyrazine; Phenazone; Methozine; Analgesine; Pyrazine; Pyrazolon.

$$C_6H_4N \begin{cases} CO.CH \\ NCH_3.CCH_3. \end{cases}$$

A synthetical base which forms salts analogous to those of ammonia.

Preparation.—According to Knorr's patent by the interaction of phenylhydrazine and acetoacetic ester, whereby phenylhydrazine acetoacetic ester is formed. By the action of heat this splits up into ethyl alcohol and phenylmethylpyrazolon, and the methylation of the latter in the presence of methyl iodide completes the process, antipyrine hydriodide being actually formed. Dimethylphenylpyrazolon is also formed direct by interaction of methyl-phenylhydrazine and acetoacetic ester.

The substitution of acetoacetic ester by other acid esters of similar constitution has also been patented. By the condensation of a halogen butyrate and phenylhydrazine, methylphenylpyrazine results, which is converted by a weak oxidising agent into dehydrodimethylphenylpyrazine, and this by methylation yields dehydrodimethylphenylpyrazine. According to recent researches (Michaelis and Lederer) the product of this method is isomeric but not identical with antipyrine; the methyl groups in the two compounds are differently related to each other, the second being represented thus:—

$C_6H_5N \begin{cases} CCH_3.CH \\ NCH_3.CO. \end{cases}$ The properties and action of the isomers

are however quite similar, save in the particulars that iso-antipyrine salicylate is difficultly crystallisable, and other salts of the two isomers exhibit differences in their physical properties.

Crotonic acid and phenylhydrazine also combine when heated to form phenylmethylpyrazolidon, which by a weak oxidizing agent is converted into phenylmethyl-pyrazolon and thence by methylation into antipyrine (Knorr). Condensation takes place very readily with a halogenated crotonate and methylphenylhydrazine, but the dimethyl-phenylpyrazolidon (hydroantipyrine) which results cannot be converted into antipyrine by oxidizing agents. An analogous condensation takes place between oxalyl-acetic ester and phenylhydrazine. Phenylpyrazolon carbonic acid ester is formed, which can be methylated and the carbonic acid driven off.

Physical and Chemical Properties.—Antipyrine occurs in odorless and colorless scaly crystals, with a somewhat bitter taste. The melting point of the pure compound is 110.5° C. (B. P. Add. 110° C.); it is readily soluble in water, rectified spirit and chloroform, but less soluble in ether (about 1 in 50). Ignited with free access of air, it burns away without residue (absence of inorganic contamination).

The absence of free acid is insured by requiring the aqueous solution to react neutral to test-paper, and of metals by providing that the passage of sulphuretted hydrogen shall produce no effect. By nitrous acid the solution is turned a green color; this is one of the tests for identity adopted by the B. P. Add. Another given by the same authority involves the production of a yellow color by the action of nitric acid, which deepens to crimson on warming, while the ferric chloride reaction—production of a deep red color, nearly discharged by excess of dilute sulphuric acid—is also inserted. This latter test distinguishes antipyrine from other organic substances which produce various colors with ferric chloride and differ in the effect of sulphuric acid upon the color.

Acetanilide has been found admixed with antipyrine. Its detection is very easy, as, though both the compounds have approximate melting points (113° C.), a mixture of equal parts

melts at 45° C. The distinguishing tests between antipyrine and its homologue, tolypyrine, are given under the latter heading.

Though a fairly stable body, antipyrine is more or less decomposed or thrown out of solution by a number of other chemical compounds and galenicals—a fact which it is of considerable importance to bear in mind in dealing with mixtures of which it forms an ingredient. From the long lists of drugs and preparations found to be incompatible with the newer substance, the following are taken as more important:—

Acid. hydrocyan. dil.
Acid. tannic.
Butyl-chloral hydras.
Chloral hydras (in strong solution).
Dec. cinchonæ.
Ext. cinchonæ liq.
Ferri sulph.
Ferric salts in solution.
Inf. catechu conc.
Inf. cinch. acid.
Inf. rosæ acid.
Inf. uvæ ursi.
Liq. arsen. et hydrarg. iod.
Mercuric chlor.
Naphtol β (solid).
Nitrites in solution, All acid.
Sodii bicarbon.
Sodii salicylas (solid).
Tinctures containing tannin, iron or quinine.
Tinct. hamamelid.
Tinct. iodi.

Phenyl-urethane and antipyrine liquefy when rubbed together (Suchanek).

Medicinal Uses.—Antipyrine is therapeutically a many-sided remedy, playing successfully the role of antipyretic, antirheumatic, antineuralgic and hæmostatic, and being employed against whooping cough, chorea, asthma bronchiale, mal de mer, etc. Externally also it has been applied as an antiseptic, and to a limited extent is applied subcutaneously.

According to Cesari, antipyrine thickens and condenses the blood without coagulating it, and hence its usefulness as a hæmostatic.

The most recent additions to the literature of the use of antipyrine in medicine treat of its value in the diarrhœa of children, in doses of ½ to 1½ grains (Saint-Phillippe); of its virtue as an antigalactagogue, in 4 grain doses every two hours (Guibert), and of its power in skin diseases, especially in such

as are attended by irritation and itching Dr. Blaschko recommends it in the urticaria-like eruptions of children; the remedy was given in powders, half teaspoonful of a 20 per cent. mixture with sugar, or in solution. The action was so favorable that the author ascribes to antipyrine a direct action on the vascular nerves. Good results were also obtained in urticaria, nervous pruritis, in true prurigo, erythema, pemphigus vulgaris, and lichen ruber. Antipyrine is to be prescribed in such cases mostly as a symptomatic remedy against itching, to be assisted by the other usual medicaments. Other favorable experience of the use of the compound in skin diseases is recorded by Prof. Saalfeld. Antipyrine has also been successfully administered in doses of 60 grains pro die in lead colic (Devie and Chatin). A favorable action on the vascular system is also ascribed to antipyrine in this case.

A powder of antipyrine 15 grains, French chalk 75 grains, boric acid 30 grains and salicylic acid 4 grains has been recommended as an effective remedy in arresting attacks of coryza (Capitan). Dr. Saalfeld strongly recommends 15 grains antipyrine combined with 45 grains potassium bromide against painful erections in chronic gonorrhœa.

In certain cases it seems that antipyrine has a tendency to cause nausea and sickness if taken internally. When this difficulty is met with, it has been recommended to administer the remedy in solution in aërated water, a form for which the free solubility of the antipyretic is a marked advantage (Dujardin-Beaumetz). The same end has been reached by the preparation of compressed tablets of antipyrine with bicarbonate of soda and tartaric acid.

It may be mentioned that the latest observations of the action of antipyrine have led to the expression of the opinion by several authorities that it has a marked, and in some instances dangerous action on the heart, producing lowering of blood-pressure, malaise and collapse (Drasche.) To the utterance of warnings to this effect must be ascribed the fact that antipyrine, which was used almost as a specific against influenza during the earlier epidemics, was almost entirely abandoned during the later. The recent report of the Therapeutic Committee of the British Medical Association shows,

however, the advantages with which antipyrine may be employed and its general freedom from ill effects.

Against the copious perspiration that frequently accompanies the action of antipyrine, atropine or agaricin are given with advantage, either at the same time as the remedy or shortly before it (v. Noorden).

As an antipyretic antipyrine is given in doses of 1¼ to 1½ drachms, in hourly portions of 15 to 30 grains. In phthisis 15 grains are given every time the temperature rises 0.2° C.; in chorea the same dose three times a day. Children are given 1½ grains for every year of age, three times, one after the other, increasing the dose if necessary (Penzoldt).

The synonyms *Pyrazine* and *Pyrazolon* are sometimes applied to antipyrine; this practice should be discouraged, as no valid excuse exists for going beyond the legitimate chemical designations and the official terms, Phenazone in England and Analgesine in France.

DERIVATIVES AND ALLIED COMPOUNDS.

Antipyrine being an alkaloidal or basic substance, readily forms compounds of definite chemical nature with acids, which may be regarded as salts of antipyrine. A number of these have been prepared, and are described in literature, but only one of them has been at all generally employed.

Antipyrine benzoate is obtained by the addition of antipyrine to a boiling aqueous solution of benzoic acid. It melts with great readiness; is little soluble in cold or in boiling water, but is very freely so in alcohol and ether. It has a pungent taste, and a slight odor of benzoic acid. The *citrate* and *picrate*, similarly prepared, have also been described.

Antipyrine salicylate, or *Salipyrine*, the only salt of the base which has so far attained any importance, is prepared by the interaction of antipyrine and salicylic acid in substance at 100° C., or in solutions. It occurs as a white, coarsely crystalline, odorless powder, with a rough but not unpleasant sweetish taste; water scarcely takes it up at all, and ether only sparingly, but it is readily soluble in alcohol (also in benzene), from which it crystallizes in hexagonal tables, with a melting point of 91.5° C.

The reaction of sodium salicylate and antipyrine, sometimes stated to be the result of a chemical change, has been decided by careful research to be merely the result of deliquescence, the salicylate acting as a carrier of moisture to the more soluble antipyrine (Spica).

Salipyrine was primarily used in acute and chronic rheumatism, and rheumatic sciatica, with good results (Guttmann, Randozza). Its chief claims to preference are based upon its comparative harmlessness—2½ drms. having been taken within three or four hours without the slightest ill-effect (Hennig)—and freedom from unpleasant by- or after-effects. Salipyrine was largely used in the epidemic influenza of 1891 to 1892, with satisfactory results (von Mosengeil, Hennig, Schreiner, Speechly, Grogrewe, Althaus). The authorities quoted especially emphasize the freedom of the action of salipyrine from cardiac influence, and see in this feature a marked advantage over antipyrine.

The remedy is administered either in powder (wafers, cachets, etc.) or in mixture, rubbed up with glycerin and flavored with raspberry syrup. In acute articular rheumatism 15 grains are given at intervals of ¼ to 1 hour until about 2 drms. have been taken. In the chronic forms of the disease large doses, beginning with 1¼ drms., are ordered the first day, increasing gradually if necessary. In all rheumatic cases the treatment is continued with smaller doses for weeks or even months after all symptoms have disappeared, in order to prevent relapse. 8 grains is often sufficient to arrest neuralgia. In influenza the dose (8 to 30 grains) is regulated according to the severity of the symptoms.

Antipyrine also forms compounds with phenols, of which two may be appropriately mentioned here, though they have as yet no medicinal importance.

Phenopyrine, prepared from equal parts of crystalline phenol and antipyrine. It is an oily liquid, free from color and odor, insoluble in cold and sparingly soluble in hot water.

Pyrogallopyrine, a crystalline compound obtained by the interaction of pyrogallol and antipyrine, in substance or in solutions. Behaves similarly to the above compound with

water, and also like it is readily soluble in alcohol and ether.

Naphtopyrine, *Resopyrine* and *Resorcylalgin* are described under **Naphtol** and **Resorcin** respectively.

Agopyrin has nothing to do with antipyrine; it is a misleading term applied to a quack remedy consisting of tablets containing ⅓ grain ammonium chloride, ⅓ grain cinchonine sulphate and 4 grains salicin.

Pelagin is an ethereal solution of antipyrine, cocaine and caffeine, that has been recommended for sea-sickness.

Antipyrine seems to be capable of forming several compounds with chloral (Choay and Béhal). One of these has been brought under the notice of the medical profession as *Hypnal*, readily prepared (Demande) by mixing a solution of 47 grammes (1½ ounces troy) of chloral hydrate in 50 cc. (1½ fluid ounces) of distilled water, with a solution of 53 grammes (1¾ ounces troy, less 22 grains) of antipyrine in 50 cc. of distilled water, pouring into a separating funnel, and drawing off, after an hour, the oily-looking liquid from the supernatant aqueous layer. At the end of 24 hours the separated liquid will have solidified to a mass of rhombic crystals, and some small rhombs will also have formed in the aqueous liquid. These should be drained and dried on bibulous paper or under a cold dessicator. They are tasteless and odorless, melt at 58° to 60° C., and dissolve in 5 to 6 parts of water.

Recommended as simultaneously hypnotic and analgesic (Bardet), 15 to 30 grains alleviating pain and inducing quiet sleep in troublesome coughs. Prescribed in aqueous mixtures, with some alcohol, flavored with orange and syrup (Bonnet). So free from taste that it can be given in 10 per cent aqueous solution without any flavoring agent (Filehne); has generally a prompt and mild action but like most hypnotics cannot always be relied upon.

Hypnal must not be confounded with **Hypnone** (*q. v.*).

Butylhypnal is a similar combination of butylchloral and antipyrine. Colorless needles, melting at 70° C., soluble in 30 parts water, easily soluble in alcohol, ether and chloroform.

Antipyrine bichloride, $C_{11}H_{12}N_2O_3Cl_2$, is formed as a white precipitate on adding chloride of lime to a hydrochloric acid

solution of antipyrine. Melts at 228° C., soluble in hot alcohol and glacial acetic acid.

Bromopyrine, the mono-bromine substitution product of antipyrine, insoluble in cold water, readily soluble in alcohol; melts at 114° C.

Iodantipyrine, or *Iodopyrine*, is a true substitution product of antipyrine, one atom of hydrogen in the benzene nucleus being replaced by iodine; hence the formula is probably $C_6H_4IN \begin{cases} CO.CH \\ NCH_3.CCH_3. \end{cases}$ The compound crystallizes in tasteless and colorless prismatic crystals, difficultly soluble in cold, but readily so in hot water; melting point 160° C.

The antipyretic activity of iodopyrine exactly corresponds to that of antipyrine; it is decomposed in the stomach into antipyrine and sodium iodide, which produce their separate therapeutical effects (Muenzer). In doses of 8 to 24 grains it reduced the abnormal temperature of typhus and pulmonary tuberculosis without any unpleasant effects; patients felt better during the use of the remedy. Very satisfactory results were obtained in a case of violent (syphilitic?) headache, cured in one day by a single dose of 15 grains, and in another of polyarthritis acuta; the latter patient was able to move about freely six hours after taking the first dose (15 grains). It would appear to be still uncertain whether iodopyrine possesses any advantages over the combined administration of antipyrine and iodide of potassium.

Isonitrosoantipyrine is the name given to the green compound produced by the action of acid nitrites on antipyrine. It was characterized as poisonous, but has been tried in medicine; reports are lacking.

Amidoantipyrine, prepared by the reduction of the above nitroso compound, and its acetyl derivative, *acetylamidoantipyrine*, are recommended for employment in medicine on account of their antifebrile properties. The former crystallises in yellow needles, melting at 109° C. and forms salts with one molecule of acids. The acetyl derivative melts at 197° C., and is easily soluble in water and alcohol.

By treating toluol solution of antipyrine with sodium and carbon dioxide, a precipitate is formed which, according to its

analysis and chemical behaviour (Bruehl and Koebner), was considered to be an *Antipyrine alcohol*, with the formula $C_{11}H_{14}N_2O$, but is now shown to be a reduction product, β-methylamido-crotonanilide, which can be synthesised from acetoacetanilide and methylamine, but cannot be reconverted into antipyrine (Knorr).

New derivatives of antipyrine have been formed by introducing alkyl or oxyalkyl groups into the antipyrine molecule, especially into the phenyl group with the intention of modifying secondary effects of the remedy. The following are the more important.

p-Methoxyphenyl-dimethyl-pyrazolon, prepared from p-methoxyphenylhydrazine and acetoacetic ester, and methylation of the resulting product. Melts at 82° C. Easily soluble in water, alcohol and chloroform, and gives isonitroso reaction. The *ethoxy* compound melting at 91° C. is quite analogous. Both show high antipyretic and antineuralgic action, but weaker than antipyrine.

Tolypyrine, or *Tolylantipyrine*, a tolyl- (or methylphenyl) dimethylpyrazolon, is prepared in an analogous manner from p-tolylhydrazine and acetoacetic ester and subsequent methylation. It differs in constitution from antipyrine in containing a third methyl group in the para position of the phenyl group. Colorless crystals, melting at 136—137° C., soluble in 10 parts of water, easily in alcohol, insoluble in ether. Tolypyrine gives the same ferric chloride, nitrous and nitric acid color reactions as antipyrine, but is distinguished from the latter by its behavior towards caustic alkalies, and higher melting point (Stock). A 2 per cent. solution of tolypyrine gives a white cloudiness with 15 per cent. caustic soda, insoluble in excess, which clears on standing, and deposits fine needles of tolypyrine; solutions of antipyrine under 5 per cent. strength remain clear. Mixtures of tolypyrine and antipyrine containing respectively 10, 25, 50 and 75 per cent. tolypyrine all melt about 94° C. An antipyretic, antirheumatic and antineuralgic of equal strength to antipyrine (Guttmann). No advantage over antipyrine (Liebreich). In neuralgia and nervous pains, enuresis, equal in action to antipyrine; in persistent migraine more successful (Dornblüth).

Tolysal, the *salicylate of tolypyrine*, is the one of many derivatives prepared from tolypyrine which has found medicinal use. Colorless crystals, melting at 101 to 102° C., scarcely soluble in water, readily soluble in alcohol. A reliable remedy in acute rheumatism of the joints in doses of 15 grains every hour up to 45 or 90 grains. Also in chronic rheumatism and rheumatic neuralgia, and free from unpleasant bye-effects (Hennig). Specially indicated in acute articular rheumatism and better borne than a combined antipyrine and salicylate of soda treatment (Dornblüth, Zurhelle). Has not the action of salipyrine in menstrual difficulties (Zurhelle).

Tolylhypnal, *monobromtolypyrine* and *mono-iodotolypyrine* have been prepared but no therapeutical reports received.

Camphopyrazolon is a compound of phenylhydrazine and camphocarboxylic acid, proposed as a substitute for camphor.

Migranin is a new antipyrine preparation possessing the composition of a double citrate of caffeine and antipyrine, but whether really a chemical compound or only a mixture is doubtful, the citrates of caffeine and similar bases being proverbially loose combinations. The three constituents, antipyrine, caffeine and citric acid, are said to be present in definite and specific proportions, the caffeine amounting to about 9 per cent. Antipyrine 89.4 per cent., caffeine 8.2 per cent., citric acid 0.56 per cent., moisture 1.84 per cent. (Hoffmann). It gives the characteristic color reactions for antipyrine and caffeine. Introduced by Overlach as a specific for migraine, and it has never failed to ward off attacks even in the most severe cases during five years' experience. Also recommended in headache with definite etiology, in the headache of influenza and of nicotine and morphine poisoning, and as a febrifuge. Employed in a number of cases of migraine that had resisted other treatment with unbroken success (Ewald). As a rule when taken during severe attacks the pain commences to abate in a few minutes and in 60 minutes is completely relieved (Bauerstein). Given in doses of 17 grains dissolved in a tumbler of water immediately preceding an attack of migraine; a second dose after two hours rarely required. The dose of 17 grains is enjoined as specific.

ARISTOL.

Synonyms: Dithymoldiiodide, Annidalin.

$$\left.\begin{matrix} C_3H_7 \\ CH_3 \end{matrix}\right\} C_6H_2(OI)-(OI)H_2C_6 \left\{\begin{matrix} C_3H_7 \\ CH_3 \end{matrix}\right.$$

A somewhat unstable amorphous powder resulting from the condensation of two molecules of thymol, and the substitution of the hydrogen of the OH group in each by iodine. It contains 45.8 per cent. of iodine. It was first introduced under the name *Annidalin*, but subsequently rechristened and again brought out.

Preparation.—Aristol is prepared by allowing a solution of iodine in potassium iodide to flow into a 10 per cent. alkaline solution of thymol at 15 to 20° C. with constant stirring. The darkish-red voluminous precipitate formed is filtered off, washed with water, and dried at ordinary temperatures. It is also said to be prepared according to a more recent patent by subjecting the mixed alkaline solutions of thymol and iodides to electrolysis, whereby iodine is first liberated and combines with the thymol.

Physical and Chemical Properties.—A brownish red, odorless, amorphous powder, insoluble in water and glycerin, slightly soluble in alcohol, and readily in ether and collodion; also taken up by fatty oils when rubbed together with them, and by vaselin. Aristol is easily decomposed by light and heat, and hence all solutions should be made without the aid of the latter, and kept from the action of the former force.

When heated in a glass tube violet iodine vapors are given off. When dried for an hour at 90° C. aristol should lose at most 1 per cent. of moisture. The aqueous extract should be neutral to litmus (absence of free alkali), leaving no residue on evaporation, and giving no blue color when fuming nitric acid and starch paste are added (absence of sodium iodide). An extract with 1 per cent. iodide of potassium solution should be colorless and give no violet or blue tint with starch paste (absence of free iodine).

Soon after its introduction, Langgaard stated that aristol gave up iodine with great readiness to substances with an

affinity for it, and pointed out that thereon depended certain restrictions in its use.

Recently manufactured specimens of this compound have been found to be less contaminated with free iodine than earlier batches, but it still contains alkaline iodide (Reuter). It may be purified from the latter by solution in glacial acetic acid, precipitating with water, thoroughly washing the precipitate, and drying at 60° C. The pale yellow product dissolves clearly and without residue in ether, and also contains no free iodine. There seems, however, some doubt as to the activity of this purified form (*v. infra*).

Medicinal Uses.—Aristol was introduced as a substitute for iodoform, over which it has the advantage of being odorless. It seems possible that the success first attained by the use of the remedy in ointment form against skin diseases was in part due to the less care taken in preparing it free from uncombined iodine and from soluble iodides. At any rate doubt has recently been thrown upon the efficacy of perfectly pure and, therefore, fairly stable aristol. Probably in the same direction lies the explanation of the unsatisfactory results sometimes obtained, such as those of Prof. Neisser, who found the substance quite inactive save in some cases of lupus, where it followed the application of a caustic.

The first observer, Eichhoff, characterized aristol as second only to iodoform in the treatment of indolent soft ulcers, and obtained in lupus such remarkable results that he believed it to be a specific poison for the bacillus of tuberculosis, while at the same time it stimulated the growth of fresh granulations (Nadaud). The experience of other observers in this disease was less satisfactory (Neisser, Schirren). It gave good results in the treatment of psoriasis (Schirren), a specially useful form being a 10 per cent. solution in flexile collodion (Schuster). In the ulcerative processes of syphilis, and in all cases where iodoform had been used, e. g., in gynæcology, dermatology, diseases of the ear, nose, pharynx, etc., aristol did good service in the hands of medical men in the principal countries of Europe. Quite recently it has been well spoken of in diseases of the ear and nose (Buerkner), in eczema and mild psoriasis (Weissblum), and in severe burns

(Stern). It has also proved an excellent remedy in the later stages of keratitis; inflammation subsides, irritation and hyperæmia of the conjunctiva and cornea disappear, and the horny tissue clears (Wallace).

It has been already intimated that some authors have not been so favorably impressed by the action of the compound; it has an undoubted advantage over iodoform in being odorless, but it appears to be inferior to it in activity (Heller). Although the perspiration and cough were sometimes alleviated in pulmonary tuberculosis by 1 per cent. subcutaneous injections, no favorable effect on the tubercular processes themselves were observed (Ochs).

The most suitable forms for applying aristol, besides the powder, are solutions in oil or ether (5 to 10 per cent.), a zinc-starch paste—which remains unchanged, though the compound is decomposed by admixture with substances having a strong affinity for iodine (Langgaard),—or ointments with lanolin or with vaselin (5 to 10 per cent.), prepared by carefully mixing the ingredients on a slab, warming gently while assiduously stirring, and straining. The liquid vaselin exerts a solvent action upon the aristol, and thus a smooth ointment results. For gynæcological application suppositories have been ordered containing 8 to 15 grains of aristol each with cacao butter. A liniment, made by dissolving 5 grains of aristol in 2 drms. of a mixture of equal parts of ether and alcohol, and incorporating 2 oz. of soft soap, is also useful in certain cases.

Apparently the prolonged employment of aristol may sometimes gives rise to chronic iodine poisoning; cases have been recorded, in which a decidedly cachectic condition was observed in patients under the treatment, which disappeared when the use of the remedy was suspended (Ewald). 1 per cent. injections do not produce toxic symptoms, but are extremely painful (Ochs).

ALLIED COMPOUNDS.

Cresol iodide is prepared in an exactly analogous manner to aristol, and on the whole closely resembles the latter in its properties. By the use of ortho-, meta-, or para-cresol the corresponding isomeric iodides are obtained.

Cresol iodide is a fine, very light powder, of yellow color, and fairly strong, but not very pleasant, odor. Very readily soluble in alcohol, ether, chloroform, and especially in fatty oils; insoluble in water. Rubbed between the fingers it has a resinous feel, and adheres to the hands and instruments so that they can be cleaned only with alcohol. In the organism mere traces of iodine are set free, so that the risk of poisoning is regarded as reduced to a minimum. Has proved useful in diseases of the nose (Petersen, Szoldeski).

Isobutyl-cresol-iodide, see under **Europhen.**

Carvacrol iodide, $C_{13}H_{19}OI$, is prepared analogous to aristol by the action of iodine upon an alkaline solution of carvacrol. It is a yellowish brown powder, almost odorless, proposed as a substitute for iodoform. It is insoluble in water, slightly soluble in alcohol, easily soluble in ether, chloroform and olive oil. At about 50° C. it softens, and at 90° C. melts to a brown liquid, but is indifferent to light and sulphurous acid.

Antiseptin, introduced as an antiseptic compound of zinc with thymol, iodine and boric acid, is simply a mixture of zinc sulphate (85 per cent.), zinc iodide (2.5 per cent), thymol (2.5 per cent.) and boric acid (10 per cent.) (Goldmann).

BENZANILIDE.

Synonym: Benzoyl-anilide.

$C_6H_5NH\,COC_6H_5$.

A crystalline compound bearing the same relation to benzoic acid as acetanilide to acetic acid.

Preparation.—By the action of benzoyl chloride or of benzoic anhydride on aniline in the presence of caustic soda, the reaction being thus represented:—

$$\underset{\text{Aniline}}{C_6H_5NH_2} + \underset{\text{Benzoyl chloride}}{C_6H_5COCl} = HCl + \underset{\text{Benzanilide.}}{C_6H_5NH\,C_6H_5CO}.$$

Physical and Chemical Properties.—Colorless, micaceous, lustrous, scaly crystals, insoluble in water, soluble

in alcohol. Melting point 163° C.; at a higher temperature distils unchanged.

Medicinal Uses.—First commended by Cahn and Hepp as an antifebrile specially suitable for children; the dose being 3 to 8 grains, according to age; and later by Kahn, of Frankfort. It produced exanthema sometimes, and apparently had not sufficiently marked advantages to insure its retention in materia medica; at any rate nothing has been added to the literature of benzanilide for a considerable time.

ALLIED COMPOUND.

Formanilide, $C_6H_5.NH(HCO)$, the corresponding compound of formic acid with aniline, is obtained by rapid distillation of 93 parts aniline with 126 parts oxalic acid, when the following reaction takes place

$$\underset{\text{Aniline}}{C_6H_5NH_2} + \underset{\text{Oxalic Acid}}{C_2O_4H_2} = H_2O + CO_2 + \underset{\text{Formanilide.}}{C_6H_5.NH(HCO)}.$$

Colorless, long prismatic crystals, melting at 46° C., and readily dissolving in water and alcohol, as well as in glycerin and oils. By dilute acids it is split up into formic acid and aniline.

Formanilide has been recommended as an antipyretic and analgesic. In doses of 2 to 4 grains two or three times daily it reduced the temperature about 2° C. in polyarthritis acuta, malaria, typhus abdominalis, etc. (Tauszk). As an analgesic in neuralgias a maximum dose of 8 grains pro die is given (Kossa). Formanilide is a better hæmostatict han antipyrine (Bokai). Besides its analgesic action it also acts as a local anæsthetic when applied to the mucous membrane in powder form or in 20 per cent. solution. 2 to 3 per cent. aqueous solution injected into the urinary tract renders cautery or the employment of the endoscope or catheter less painful (Meisels). Mixed with equal parts of starch, it serves as an insufflation in pharyngeal and laryngeal affections, a burning sensation is produced for a few minutes after insufflation, followed by an analgesia of 8 to 12 hours duration (Preisach). So far, however, the remedy has not come much into use.

BENZOSOL.

Synonym: Benzoyl-guaiacol.

$C_6H_4OCH_3OCOC_6H_5$.

A crystalline compound of guaiacol in which the hydrogen atom of the hydroxyl is replaced by benzoyl.

Preparation.—By formation of a potassium salt from crude guaiacol and purification of the salt by re-crystallization from alcohol. The pure product is then warmed with the calculated amount of benzoyl-chloride, and the resultant benzosol re-crystallized from alcohol. Also by the interaction of guaiacol with benzoic anhydride.

Physical and Chemical Properties.—A colorless crystalline powder, almost odorless and tasteless. Melting point 50° C. Absolutely pure benzoyl-guaiacol melts at 59° C. (Thoms). Insoluble in water, readily soluble in hot alcohol, in ether and in chloroform. It contains 54 per cent. of guaiacol. The melting point of benzosol should not be below 44° C. (Bongartz), and when allowed to remain in contact with sulphuric acid, even for prolonged periods, only a pale yellow coloration should be produced. When saponified with alcoholic potash a pure guaiacol odor should be developed. Benzosol is distinguished from salol by the fact that it gives a purple-red color when treated with concentrated sulphuric acid in the presence of acetone, whilst salol assumes a yellow color with a shade of red.

The products of the decomposition of benzosol in the organism (its constituents) can be readily detected in the urine and saliva of patients under treatment (or even half an hour after a single dose); the secretion is distilled with diluted sulphuric acid, the clear distillate (in which the guaiacol can be detected by the sense of smell) is placed in a test tube, and to it is added a small quantity of a highly dilute solution of liquor ferri sesquichlorati (2 to 3 drops to a test tube full of water). In the presence of guaiacol a reddish-brown color is gradually developed, the intensity of which is proportional to the amount of the compound in the solution. It can be detected by the same method in the perspiration.

Medicinal Uses.—The therapeutical value of benzosol in the treatment of phthisis depends upon its content of guaiacol, which appears to be set free by the alkaline juices of the intestinal tract, being excreted as combinations of guaiacol and benzoic acid with the urine. Its advantage over the parent substance (guaiacol) is of course its comparative freedom from taste, so that it can be given in large doses—an essential of the so-called intensive guaiacol treatment of phthisis—without the disturbance of the digestive functions or disagreeable eructations caused by the former as liquid in mixtures, while at the same time free from the local irritant effect sometimes ascribed to the capsules, and superior to pills in readiness of absorption.

In doses of 4 grains, gradually increasing to 12 grains, three times a day (equal to about 24 grains of creosote), results were obtained in the treatment of phthisis equal if not superior to those yielded by creosote (Walzer). The action of the remedy in ten closely observed cases soon manifested itself in a decrease of the number and violence of the fits of coughing, a diminution in the expectoration, and disappearance of hectic perspirations. The appetite, and with it the general condition and well-being, speedily improved, as was evidenced by the increase of body-weight. The remedy can be taken for long periods without disturbance, but is to be avoided in feverish patients (Hughes).

Benzosol has also been recommended in diabetes as a specific in reducing the quantity of urine, its specific gravity and percentage of sugar (Wiktor, Piatzowski). In eight patients to whom 45 to 75 grains were administered daily the decrease of sugar in the urine is said to have corresponded to the increase in body-weight. Later authors (Palma, Lins) fail to observe any specific improvement in diabetic cases closely observed under administration of benzosol, but the remedy exercises a beneficial influence on the general nutrition, and consequently increases the resistance of the patient to the disease. Polarimetric sugar determinations in urine are incorrect after the administration of benzosol (Jolles).

The compound is given in powder, in pastilles of sugar and chocolate, or with addition of oil or spirit of peppermint.

Benzosol has been put upon the market by more than one firm, and there is reason to believe that the products are different. At least one of them is reported by Professor Sahli to have a different smell and odor to that described above, and this in large doses (1½ to 2 drachms daily) and with continued use had no effect at all upon tuberculosis. Sahli concluded that the effects of guaiacol and creosote were due to local antiseptic action in the stomach, and hence would not be substituted by benzosol, but this view is not supported by the experience of others with the treatment. (*Cf.* **Guaiacol**—*Medicinal Uses.*)

BETOL.

Synonyms: Naphtalol; Naphtosalol; Salinaphtol.

$C_6H_4OH\ COOC_{10}H_7$.

A crystalline compound, with the composition of a β-naphtol salicylate, and closely allied to salol.

Preparation.—By heating together a mixture of β-naphtol-sodium, sodium salicylate and phosphoric chloride; besides betol, sodium meta-phosphate and sodium chloride are formed.

Physical and Chemical Properties.—When pure, betol forms a colorless, odorless and tasteless, lustrous, crystalline powder, melting at 95° C. Insoluble in water or glycerin, soluble with difficulty in alcohol and turpentine, readily in boiling alcohol (1:3), ether, benzene, and in warm linseed oil.

Betol is a fairly stable body, unaffected in the cold by alkalies or acids (unless very strong); when heated with these reagents in strong solutions it splits up into β-naphtol and salicylic acid. The same effect is produced by the alkaline pancreatic juice and other intestinal ferments, but the acid secretions of the stomach have no effect upon it. It appears in the urine as salicylic acid and naphtol glycuronate.

Absence of free salicylic acid is proved by pouring a few drops of an alcohol solution into very dilute ferric chloride solution, when no color should be produced The compound is distinguished from salol by its much higher melting point (salol = 43° C.), and by the production of a pure lemon-

yellow colored solution with pure concentrated sulphuric acid, which a trace of nitric acid changes to olive brownish-green. With salol no such color results.

Inorganic impurities, chlorides, phosphates, etc., are detected in the usual manner. Impure preparations are said to assume a blue or reddish tint on keeping.

Medicinal Uses.—At first it was expected that betol would prove equally as valuable as salol, but its higher melting point and chemical stability proved to be disadvantages which restricted its use. At the same time its lower degree of solubility also told against it, and although it was used internally as powder in vesical catarrh, articular rheumatism, etc., (5 to 6 grains four times a day), instead of sodium salicylate (Kobert), and externally in the form of bougies (1:4 of cacao butter) in the treatment of gonorrhœa, it seems now to have been almost entirely forgotten.

ALLIED COMPOUND.

Alphol, the corresponding salicylate of α-naphtol, is prepared by the process common to all the salol compounds, of heating a mixture of sodium salicylate, α-naphtol sodium and phosphoric oxychloride to 120° or 130° C. The product of the reaction is extracted with water, to remove the sodium chloride and sodium phosphate formed, and the organic salt recrystallized from alcohol. Alphol is split up by the intestinal juices in an analogous manner to salol and betol. It is employed in 8 to 15 grain doses in articular rheumatism and gonorrhœtic affections.

BROMOFORM.

Synonym : TRIBROMOMETHANE.

$CHBr_3$.

An analogue of chloroform, discovered in 1832 by Löwig.

Preparation.—By the action of bromine upon a solution of equal parts of caustic potash and methyl alcohol. The separated bromoform is washed with sodium carbonate solution, freed from water with calcium chloride, and rectified.

Just as iodoform and chloroform have recently been prepared from acetone, so a process has been devised (Denigès) for the production of bromoform. Bromine is added to soda solution artificially kept cool; bromide and hypobromite of sodium are formed thus:

$$6\,Br + 6\,NaHO = 3\,NaBr + 3\,H_2O + 3\,NaOBr$$

Sodium hypobromite.

Acetone is then brought into contact with the mixture when (even in the cold) reaction takes place, the by-products being acetate and hydrate of sodium:

$$3\,NaOBr + CO(CH_3)_2 = CHBr_3 + CH_3COONa + 2\,NaOH$$

Acetone — Sodium acetate.

The yield amounts to about 60 to 70 per cent. of the theoretical quantity.

Physical and Chemical Properties.—A clear, colorless liquid when pure, with a peculiar but not unpleasant odor, and a sweet taste. Specific gravity 2.9, and boiling point 147 to 148° C., (149 to 150° C., Denigès). Bromoform is only very slightly soluble in water (8 or 10 drops in 6 ounces of water), but readily in alcohol. When evaporated by gas or lamp-light, bromine and a bromine compound ($COBr_2$)—very irritating to the mucous membrane of the throat and conjunctiva—are apparently produced, analogous to the chlorine and phosgen gas formed from chloroform under similar conditions.

Bromoform for medicinal use must be free from acid and color. Yellowish specimens are unfit for administration until they have been purified by washing with dilute soda solution and drying over calcium chloride. Pure bromoform also does not attack the mucous membrane like chloroform. It must be kept out of sunlight.

Medicinal Uses.—Bromoform was warmly recommended in 1889, as a remedy for the whooping cough of children, in daily doses of 5 to 20 drops, dissolved in 4 ounces of water with addition of spirit.

℞ Bromoformi ..... gtt. x.
Spir. vini rect. ..... ♏ 45 to 60
Syrupi ..... q. s.
Aquæ dest. ..... ad. ℥ iv.
M. S. To be taken during the day.—(Stepp.)

The same author afterwards prescribed the remedy unmixed, so many drops being ordered to be taken in water, coffee, or the like. Equally favorable results were obtained by others (Senator, Lœwenthal, Schippers, Cassel), and from the experience of some hundreds of cases, bromoform was pronounced to be harmless, and to have a marked effect in promptly diminishing the number and violence of attacks, the excretion of mucus and the duration of the disease, while also vomiting and bleeding from the mouth and nose were arrested. According to Neumann, the action is very often good, but the remedy is no specific.

The pleasant taste of the compound—an undoubted advantage in the treatment of children—has also proved a source of danger. Cases have been described in which the little patients, tempted by the nice flavor of the medicine, obtained access to the bottle and drank the whole contents, equivalent sometimes to 20 or 30 drops of bromoform. Deep narcosis supervened, preceded by a short stage resembling alcoholic intoxication. Injections of ether in one instance, and fresh air with prolonged practice of artificial respiration in another, were eventually successful, and the patients on recovery felt quite well. It is evident that the dosage should be carefully restricted, and it would seem advisable not to adopt the practice of sending out the unmixed bromoform.

According to recent researches on animals, inhalations of bromoform have an anæsthetic effect similar to that of chloroform (Rabuteau); the narcosis seems, however, to be of shorter duration.

Good results have been recorded from the external application of the liquid as an analgesic and antiseptic(Solis-Cohen). Ozæna and tuberculous and other ulcers of the larynx were successfully treated by the local use of bromoform, the affected areas having been previously cleansed by hydrogen peroxide. As the substance is volatile the effect was transient, and the author recommends to follow with the application of iodoform.

BROMOL.

Synonym : TRIBROMOPHENOL.

$C_6H_2Br_3OH$.

A compound well-known to the chemist, being produced in one of the processes used for the estimation of phenol or carbolic acid.

Preparation.—When dilute solutions of phenol are precipitated with bromine water a crystalline precipitate is formed, consisting of carbolic acid in which three atoms of hydrogen in the phenyl group and that of the hydroxyl group are replaced by bromine; on solution in alkali, and reprecipitation with acid, tribromophenol is formed.

Physical and Chemical Properties.—When pure, bromol forms white crystals, melting at 95° C., practically insoluble in water, but freely taken up by alcohol, ether, and chloroform; also soluble in glycerin, in fatty and essential oils. The odor is unpleasant, bromine-like, and the taste sweetish-astringent.

Tribromophenol was bacteriologically investigated by Grimm, in 1888. "Bromol" is recommended to be used in solution (1:30 olive oil) or ointment (1:10), as powder or dressing. Against diphtheria a 4 per cent. glycerin solution is to be used. In doses of one-tenth to one-third grain it has been given in cholera infantum and typhus abdominalis as an intestinal disinfectant.

DERIVATIVES AND ALLIED COMPOUNDS.

Chlorphenol. Under this term a liquid, described as very volatile, and giving off vapors specifically heavier than air, has been recommended for inhalation in pulmonary tuberculosis and other d seases of the respiratory organs. The inhalation liquid consists of 7 parts of a chlorinated phenol (probably orthomonochlorphenol) and 3 parts of a mixture of alcohol, eugenol and menthol; 16 to 30 drops are inhaled daily, the heavy vapors penetrating into all recesses of the lungs, and there exerting their antiseptic action (Passerini). Chlorphenol has also been used as an application to wounds, indolent ulcers, etc. Cures are recorded from the treatment in five cases of incipient pulmonary tuberculosis (Passerini).

Para-Monochlorphenol, $C_6H_4Cl(OH)$, possesses the greatest antiseptic power of the three isomeric mono-chlorine derivatives of phenol, all of them prepared by direct or indirect chlorination of phenol. It is a crystalline body, melting at 37° C., and easily soluble in alcohol, ether and alkalies, but sparingly so in water. Employed successfully as a 1 to 2 per cent. ointment in erysipelas; rubbed in twice a day it lowers the temperature about 2° C., removes congestion, prevents spreading, and does not irritate the skin (Tschuriloff).

Ortho-Monobromphenol, C_6H_4BrOH, is a dark violet liquor of strong odor, boiling at 194° C. It is soluble in alcohol, ether and alkalies, and also in water to the extent of 1 to 2 per cent. Its therapeutical indications are the same as for monochlorphenol. Twenty cases of erysipelas under this treatment were cured in 3 to 6 days on the average, only one case persisting for eight days (Tschuriloff).

Chlorol is not an organic chlorine compound corresponding to bromol, but the name is given to an antiseptic solution of mercuric and sodium chlorides, to which copper sulphate is added to act as an emetic in case of accidental swallowing.

Tribromphenolate of Bismuth, $(C_6H_2Br_3O)_2BiOH + Bi_2O_3$, is a yellow, neutral, insoluble powder, free from taste and odor, and containing 50 per cent. bromol and 50 per cent. bismuth oxide. The tribromphenolate is without action on the mucous membrane, or on the digestive organs. It possesses extraordinary antiparasitic properties, which together with the absence of toxicity makes it an excellent intestinal antiseptic and a specific against cholera (Hueppe). In doses of 8 grains given as a powder about every two hours.

Gallobromol is dibromo-gallic acid, $C_6Br_2(OH)_3COOH$. It occurs in fine, white needles, soluble in hot water, alcohol and ether. Cold water dissolves about 12 per cent. of its weight. Gallobromol is a germicide and antiseptic, which has been employed with great advantage in the treatment of blennorrhagia (Cazeneuve, Rollet, Quilly). It is indicated in all stages of blennorrhagic urethritis in solutions of 2 to 4 per cent. strength for irrigation of the urethra and bladder; for injections into the anterior portion of the urethra solutions up to 10 per cent. strength may be employed during the abortive

period. Owing to the large amount of bromine present gallobromol has a very sedative influence on pain and erections. Cystalgia accompanying micturition is also relieved. Gonococci disappear after four or five days' treatment, and chronic blennorrhagia of months' standing has yielded in the course of a few days. The aqueous solution is best prepared fresh, as a slow decomposition takes place with liberation of hydrobromic acid on standing. Gallobromol is also recommended therapeutically as a substitute for potassium iodide, as the depressant action of the latter is absent (Lépine). It has been successfully administered in doses of 30 to 45 grains, given in sweetened water, once daily, as a sedative in various nervous diseases; but even three or four drachms can be taken without deleterious symptoms arising.

Gallanol, see under **Gallacetophenone.**

CHINOLINE.

C_9H_7N.

A tertiary amine, first prepared by the distillation of quinine or of cinchonine, and subsequently synthesised by Bæyer, Königs, and others.

Preparation.—Either by extracting the elements of water from hydrocarbostyril with phosphorus pentachloride, or by the action of caustic soda upon the mixture of acrolein, nitrobenzene and aniline, formed when nitrobenzene, aniline, glycerin and sulphuric acid are heated together. The chinoline obtained is purified from unaltered aniline by fractionation and precipitation from alcoholic solution as sulphate, or by ebullition with chromic acid.

Physical and Chemical Properties.—Pure chinoline is a colorless liquid with a pungent characteristic aromatic odor. Specific gravity at 15° C., 1.084; boiling point 237° C. Very slightly soluble in cold water (though hygroscopic), more readily in hot water, and freely in alcohol, ether and chloroform. By the action of light and air chinoline is rapidly turned brown; it is decolorized by shaking with solid

potash or soda and slow rectification. Chinoline by direct addition of acids forms crystalline salts which are mostly hygroscopic, and double salts with the metals. By the action of fuming sulphuric acid the base is converted into chinoline sulphuric acid, which, when melted with potash, yields oxychinoline, C_9H_6NOH.

Evidently the compound may be contaminated by water (which lowers the boiling point), by homologous compounds (which raise it), by aniline or nitrobenzene and hydrocarbons. Aniline, if present, gives a violet color with chlorinated lime solution, and nitrobenzene or the hydrocarbons separate as oily drops when the base is mixed with excess of concentrated sulphuric acid and cooled.

Medicinal Uses.—Chinoline is antiseptic, antizymotic and antipyretic (Donath); 0.2 per cent. prevents the putrefaction of urine, 0.4 per cent. that of blood. Subcutaneously injected into animals it lowers the body heat; doses of 15 to 30 minims *pro die* were recommended for human beings, but not much employed. Has been found useful for local application in pharyngology (Seifert), and for the disinfection of the cavities left after the extraction of carious teeth (Scheff). Cotton wool is soaked in pure chinoline, pressed into the canal, allow to remain 24 hours and renewed; perfect asepsis is attained in two or three days.

DERIVATIVES AND ALLIED COMPOUNDS.

Chinoline bisulphate, hydrochloride, salicylate, tannate and tartrate have been recommended. The two chief salts are described below:

Chinoline salicylate, a white, crystalline powder, soluble in water (1:8) and in glycerin; very soluble in alcohol, ether, vaselin, and fatty oils.

Chinoline tartrate occurs in long white rhombic crystals, with a faint amygdaloid odor; it has the advantage over most chinoline salts of being non-hygroscopic. 70 to 80 parts of cold water are required for solution, but less of hot water. In 5 per cent. solution, it has been successfully employed in whooping cough (1½ grains every three hours —Koch and Seifert), and in doses of 15 grains, in two or

three portions, three hours before the attacks, in intermittent fever (Loewy). According to Brieger, however, chinoline has no useful action, but on the contrary irritates the stomach.

Kairin, or ethyl-kairin, $C_9H_{10}(C_2H_5)NOHCl$, prepared from chinoline, through α-chinoline sulphonic acid, α-oxy-chinoline and α-oxychinolinetetrahydride, was one of the first substitutes for quinine prepared by synthesis. It was recommended by Filehne, in hourly doses of 5 to 8 grains, or single doses of 15 grains, as an antifebrile, but its use was attended with considerable risk; subsequently it was displaced by the antipyretics later discovered, and now is no longer manufactured.

The so-called *Kairin M.* was hydrochloride of α-oxychinolinemethyltetrahydride, $C_9H_{10}(CH_3)NOHCl$, whilst *Kairolin A.* and *Kairolin M.* were the acid sulphates of ethylchinolinetetrahydride and methylchinolinetetrahydride respectively.

Acetylorthoamidochinoline, $C_9H_6N(NHCH_3CO)$, an analogue of acetanilide in which chinoline plays the part of benzene nucleus, is prepared in analogous manner from chinoline by nitrification, reduction and acetylisation. It occurs in the form of colorless crystals, melting at 102.5° C. It gained passing notice as an antipyretic, but did not secure a permanent position. The ethoxy derivative of acetyl- and especially of benzoyl-amidochinoline has gained a reputation under the name of **Analgene** (q. v.).

Diaphterin, or *Oxychinaseptol*, is a loose, unstable compound or mixture of one molecule ortho-phenolsulphonic acid (sometimes called by the trivial name *aseptol*) and two molecules ortho-oxychinoline. It is prepared by saturating the phenolsulphonic acid with the calculated quantity of oxychinoline and is therefore given the formula

$HO.C_9H_6N$	$HSO_3.C_6H_4.OH$	$C_9H_6N.OH$
Oxychinoline	Phenolsulphonic Acid	Oxychinoline.

It forms large hexagonal crystals when crystallized from water, is very soluble in water, and melts at 85° C. The aqueous solution is colored bluish-green with ferric chloride. Diaphterin possesses an equal bactericidal action to carbolic acid, and has the advantage that it is easily soluble and comparatively non-poisonous (Emmerich). It cannot be

used to sterilize iron or nickel instruments, and colors the nails yellowish (Stabel). Has been successfully employed in general surgical practice in ½ to 2 per cent. aqueous solution (Kronacher). The wounds were maintained clean and free from irritation or eczema and healed quickly. Very useful in solution for purulent affections of the ear and nose, and also for insufflation (Rohrer). In dental practice ½ per cent. solution is employed as a wash after extraction, etc. (Harnecher).

Diaphtol, or *Chinaseptol*, $C_9H_6(OH)(SO_3H)N$, is ortho-oxychinoline-meta-sulphonic acid, and is the aseptol of the chinoline series, standing in the same relation to chinoline as phenolsulphonic acid to benzene. It is prepared by the action of concentrated sulphuric acid on ortho-oxychinoline. It occurs in yellowish-white crystals, which are only sparingly soluble in cold water, but dissolve in about 35 parts of boiling water. The crystals melt at 295° C. The aqueous solution gives a fine green color with ferric chloride. Diaphtol is without irritating action either by internal or external employment, prevents putrefactive decomposition of the urine better than salol, and is, therefore, specially indicated for disinfection of the urinary and sexual organs (Guinard).

Loretin is the meta-iodo-ortho-oxychinoline-ana-sulphonic acid, $C_9H_4(I).(OH)(SO_3H)N$, discovered by Professor Claus, which not only combines the characters of a phenol, sulphonic acid and chinoline derivative, but also as an iodine preparation, is indicated as a powerful antiseptic. It is prepared by boiling a mixture of equal parts of ortho-oxychinoline-ana-sulphonic acid, potassic carbonate and potassium iodide with water and the amount of chloride of lime corresponding to one atomic equivalent of active chlorine. The iodo acid separates as an orange-red crystalline powder, consisting of the insoluble calcium salt. This salt is washed and decomposed with hydrochloric acid, whereby the free acid is liberated and purified by conversion into the soluble sodium salt and reprecipitation with dilute mineral acids.

Meta-iodo-orthooxychinolinesulphonic acid is a pale yellow crystalline powder, only very slightly soluble in water (1 or 2 parts per 1000) and alcohol, insoluble in ether, benzene, chloroform and oils. It browns at 250° C., and melts and

decomposes at 280° C., leaving no ash on incineration. Concentrated sulphuric acid dissolves it unaltered. Fuming nitric acid dissolves it with evolution of iodine vapors and precipitation of dinitrooxychinoline on dilution with water. The acid forms soluble neutral and basic salts with alkalies and neutral magnesium and aluminium salts. The salts of other metals are quite insoluble or soluble less than 1 per cent.

Loretin has been introduced as a substitute for iodoform, which it resembles in appearance; it is completely inodorous. Employed in the treatment of boils, whitlows, burns and lacerated wounds, in gynæcological practice and in major operations, without a single instance of toxic effect or death (Schinzinger). It is devoid of irritant effect on the skin, cures eczema, and surpasses the action of iodoform in its favorable action on the process of granulation and healing. Antiseptic and deodorant. Employed also with success in veterinary practice (Metz, Fenzling). Loretin is non-toxic and causes no renal irritation (Ammelburg).

Loretin may be employed as a dusting powder, either alone or with diluents; in 2 to 10 per cent. collodion emulsions for erysipelas and application after cautery of the nose; in 5 to 10 per cent. ointments or cocoa butter pencils, and in 0.1 to 0.2 per cent. aqueous solutions. Stronger solutions (1 to 5 per cent.) can be prepared with the sodium salt, and loretin gauze for bandages by steeping the gauze in a solution of the sodium salt, and then in calcium chloride, whereby the insoluble red calcium salt is precipitated in the texture.

CHLORALAMID.

Synonym: CHLORAL-FORMAMIDE.

$CCl_3CH.OH.CONH_2$.

Preparation.—By the interaction of chloral (not chloral hydrate) and formamide at ordinary temperature, according to the equation

$$\underset{\text{Chloral.}}{CCl_3CHO} + \underset{\text{Formamide.}}{CHONH_2} = \underset{\text{Chloralamid.}}{CCl_3CH.OH.CONH_2}.$$

Physical and Chemical Properties.—Lustrous, colorless crystals, with a somewhat bitter taste. Melting point 115° C.; at a higher temperature it dissociates into its components. Slowly soluble in about 20 parts of cold water, or in 1½ parts of 96 per cent. alcohol. By water heated over 60° C. it is decomposed into chloral hydrate and ammonium formate.

Chloralamid contains 76.6 per cent. anhydrous chloral and 23.4 per cent. formamide, and answers to tests for either. Dissolved in 9 parts alcohol the solution does not redden litmus paper (absence of free formic or hydrochloric acids), but the aqueous solution reacts faintly acid. The alcoholic solution does not at once produce a precipitate with silver nitrate (absence of free formamide, hydrochloric acid), but after a short time a red color appears from reduction of the silver nitrate. Volatilizes completely without evolving inflammable vapors (absence of chloral alcoholate). Warmed with caustic soda solution it becomes turbid owing to the separation of chloroform.

Medicinal Uses.—Chloralamid was recommended by von Mering as a substitute for chloral hydrate, being slowly decomposed into its constituents in the blood, when the formamide by its stimulant action upon the vascular centres counteracted the fall of blood pressure brought about by the chloral. The compound has been largely and widely adopted as a hypnotic, on the whole with very satisfactory results (Kny, Reichmann, Hagen and Hüfler, Rabow, Alt, Patterson, White, Strahan, Gordon, Atkinson, Collins, Wood, Clevenger, Barr, Egbert), the authors agreeing that the remedy has no injurious action on the heart, that it is effective even when the patients are suffering from painful diseases, and the sleep produced is light and refreshing. Some of the observers named regard chloralamid as "the ideal hypnotic, free from all unpleasant or dangerous by- or after-effects" (Atkinson).

Physiological research has shown: 1. that chloralamid acts more powerfully upon the cerebral cortex than upon any other portion of the nervous system of voluntary life, thereby causing sleep and muscular relaxation; 2. that in moderate doses it stimulates the respiration; and 3. that it has a very feeble influence upon the circulation (Wood, Piccinimo). Its

physiological action has also been described as exactly similar in kind to that of chloral hydrate (Mairet and Bosc), but also as of nutrient character (Clevenger).

Evidence is abundant that in practice there is a real distinction between the effect of the older hypnotic and its newer derivative. Cases are recorded, in which the nervous system, "almost entirely wrecked," has been improved in tone by the quiet refreshing slumber induced by chloralamid, where chloral hydrate had failed (Mattison).

The combination of the amido group with chloral is calculated to combine the stimulating action of ammonia with the soporific action of chloral, and thus prevent any danger arising from the depressing effects of chloral on the heart, which appears practically to be the case (Lauder Brunton).

The remedy is without any ill-effect upon the digestive processes (Gordon), and distinctly promotes the digestion of flesh diet (Penzoldt).

Very satisfactory results have been yielded by chloralamid in the treatment of the insomnia of alcoholism (Helm, Hexamer, Egbert), of mental disorders generally (Naecke, Wright, Umpfenbach, Barbour), in gynæcology (Denhard, Dupon), especially in aggravated cases with hysterical convulsions, in senile insomnia, pulmonary diseases, neuralgia, and hysteria (Gordon, Charteris, Therapeutic Committee of the British Medical Association).

That the remedy may be given with safety, even when the heart is affected, is demonstrated by a number of cases. In one of them the patient (an old lady of 60 years) had suffered from heart disease for eight years, and was troubled with dyspnœa, cough and insomnia. Morphine was first tried without any great benefit, and then chloralamid was given in 10 grain doses, gradually increased to 40 grains. Better and longer rest was thus obtained, and the pulse improved (Patterson). It does not lose its effect by prolonged administration (Barbour, Egbert).

Chloralamid is useful to quiet the nervous system, and to produce sleep after major operations. For this purpose it is "the ideal sedative, giving prompt and satisfactory action,

without the disadvantages of chlôral, morphia, and other narcotics" (Lanphear).

A recent publication from America deals with conclusions based on the treatment of nearly 300 cases with chloralamid, given in a mixture similar in strength to that cited below (but containing tincture of cardamoms for spt. frumenti, and syrup of orange as well as of raspberries). The conclusions are eminently favorable and confirm those of the other authors who recommended the remedy (J. Wood).

Subcutaneously administered (4 per cent. aqueous solution) quiet and refreshing sleep, lasting for about eight hours, was induced by one or two syringefuls (each of 15 minims) in carcinoma of the rectum with violent pain, and in severe hepatic colic (E. Schmidt).

The dose of chloralamid is 15 to 40 grains, and it should be prescribed and dispensed only in solution. Further, it is necessary to point out that as hot water decomposes the compound it must always be dissolved in the cold. The addition of spirit, in which chloralamid is freely soluble, facilitates the preparation of mixtures. An approved formula is:

℞ Chloralamidi ..... ʒ ii
Spt. Frumenti ..... ℥ i
Ft. solut. et adde
Syr. Rubi idæi ..... ℥ i
M. S. One tablespoonful, to be repeated in one hour if sleep be not produced.

Any flavoring syrup may be substituted for the syrup of raspberry, or glycerin and tincture of ginger, cardamoms, or an aromatic water may be added. The liqueur "Bénédictine" (1 to 2 drms. to each ounce of water) is also a good and agreeable corrective (Atkinson).

The freedom of chloralamid from noxious effects renders it suitable for children in the sleeplessness of acute infectious disorders. Marcus prescribes:

℞ Chloralamidi ..... ʒ j
Liq. Ammon. acet. ..... ℥ ss
Syrupi simplex ..... ℥ ij
Aqua ..... ℥ iv
M. S. For a three year old child one teaspoonful to be taken every four hours.

Chloralamid may be effectively prescribed in solution with bromide of potassium (Charteris). Under the name of *Chlorobrom* a solution of chloralamid is sold in England, consisting of 6 parts chloralamid and 6 parts potassium bromide in 88 parts of water, concerning which an overwhelming literature exists as to its efficacy as a gastric sedative. It is recommended as a prophylactic and an almost infallible remedy for sea-sickness, especially for the after-retching, in doses of one tablespoonful for females, and one and a half tablespoonfuls for males, before retiring to rest, or in teaspoonfuls every ten minutes until vomiting ceases (Charteris, and reports of numerous ship surgeons). Also in doses of 30 to 60 minims in persistent vomiting not arising from sea-sickness, and as a relief in gastric ulcers (Masters).

DERIVATIVES AND ALLIED COMPOUNDS.

Chloralammonium, $CCl_3CH(OH)NH_2$, sometimes called *chloral-amide*, but not to be confused with the above chloralamid or chloral-formamide. A white crystalline powder consisting of small needles, with a melting point between 60° and 64° C. Prepared by leading dry ammonia gas into a solution of anhydrous chloral in chloroform (Schiff). It is soluble in water, but the solution is very prone to change. The substance is said to be split up even in the solid state. Has been given as a hypnotic in doses of 10 to 30 grains, and is described as combining the properties of urethane and chloral hydrate, but having a less marked action on the heart and respiratory centre than the latter (Nesbitt).

Chloral-urethane and *Ethylated Chloral-urethane*, or *Somnal*, *vide* **Urethane.**

Chloralimide is a chloral derivative, prepared by the action of heat on chloralammonium, or by heating chloral hydrate with dry ammonium acetate. The formula of this compound, (which must not be confounded with chloralamide), is given as CCl_3CHNH; it occurs in long crystalline needles, without color, taste or odor; melting point about 166° C.; insoluble in water, soluble in alcohol, and more in ether, in chloroform and in fatty oils. Chloralimide is very stable, being unaffected by light, air or moisture. It was introduced as a sub-

stitute for chloral hydrate, to which it was said to be superior in activity (Choay), but it has been practically discarded and is no longer prepared.

Chloraloximes are a new class of compounds of chloral with oximes, the products of the reaction of hydroxylamine with aldehydes and ketones, which have recently been recommended as hypnotics. The following chloraloximes have been prepared: *chloralacetoxime,* $(CH_3)_2$:NOCH(OH).CCl_3, melting at 72° C.; *chloralacetaldoxime,* CH_3CH:NOCH(OH)-CCl_3, melting at 74° C.; *chloralbenzaldoxime,* C_6H_5CH:NOCH-(OH)CCl_3, melting at 62° C.; *chloralcamphoroxime,* $C_{10}H_{16}$:-NOCH(OH)CCl_3, melting at 98° C.; and *chloralnitrosobeta-naphtol,* $C_{10}H_5$(OH):NOCH(OH)CCl_3, melting at 100° C. All these compounds are crystalline substances, easily soluble in alcohol and ether, and decomposed by hot water into their constituents. In the organism the chloraloximes suffer a similar decomposition into oximes and chloral hydrate, the latter of which exerts the hypnotic action. The dosage of the new remedies has not yet been determined.

Chloralose, or *Anhydroglucochloral,* $C_8H_{11}Cl_3O_6$, is the name given to a compound of chloral with sugar. Prepared by heating a mixture of equal parts anhydrous chloral and grape sugar for one hour at 100° C. The following reaction takes place:

$$\underset{\text{Chloral}}{CCl_3CHO} + \underset{\text{Glucose}}{C_6H_{12}O_6} = H_2O + \underset{\text{Anhydroglucochloral.}}{C_8H_{11}Cl_3O_6}$$

The product of the reaction is extracted with ether, water added to the ethereal residue and distilled with steam until all uncombined chloral is driven off. The subtance is then separated by crystallization into α-anhydroglucochloral (Chloralose) and β-anhydroglucochloral (Parachloralose).

Chloralose occurs in fine colorless needles, melting at 184 to 186° C. It dissolves in 170 parts water at 15° C., more easily in hot water, very readily in alcohol, ether and acetic acid. The crystals possess a bitter taste. Introduced as a hypnotic as a substitute for chloral, free from the unpleasant bye-effects upon the heart and from the cumulative action of of the latter (Hanriot and Richet). The action of chloralose is due to diminished sensibility of the grey matter of the

brain. Has been successfully employed in neurasthenics, tabes, diabetes and mental disorders (Feré, Maragliano, Morselli, Scaze, Rossi). In doses of 1½ grains at commencement of treatment, to be repeated until the desired result is obtained. Contraindicated in hysteria, in which small doses produce unpleasant nervous symptoms. Not constant in its action and, therefore, administration attended with a certain amount of danger (Lang).

Parachloralose, $C_8H_{11}Cl_3O_6$, has the same empirical composition as chloralose, and is either isomeric or polymeric with the latter. Crystallizes in shiny tablets, melting at 229° C., and soluble in hot alcohol, ether and acetic acid, but insoluble in cold water and sparingly in hot.

Caffeine-chloral, $C_8H_{10}N_4O_2.CCl_3CHO$, a combination of chloral and caffeine in equal molecular proportions. Colorless glassy crystals, soluble in water. Possesses a sedative and analgesic action upon irritated conditions of the peripheric system, whilst also acting as a mild laxative in constipated conditions (Ewald). Its analgesic action has been demonstrated in rheumatic affections, sciatica, gastric ectasis and emphysia. Its usefulness where a narcotic action is required free from the constipating action of opium preparations, has recently been recognized by several authors (Neumann, Morvay, Rachel), who remark upon its reliable laxative properties, and freedom from deleterious bye-effects. Administered subcutaneously in doses of 3 to 5 grains in concentrated aqueous solution two or three times a day. The injections are painless.

CRESALOLS.

Synonyms: Cresol Salicylates. Cresolsalols.

$C_6H_4OH\ COO\ C_6H_4CH_3$.

Ortho-, meta-, and para-cresalol are crystalline esters, analogous to betol and salol.

Preparation.—By heating together at a high temperature molecular weights of the salicylate and of the cresylates of sodium with phosphoric chloride, a cresalol (ortho, meta or

para according to the sodium salt used) is formed as well as sodium chloride and phosphoric anhydride. The product is treated with water, which removes the sodium salt and the phosphoric anhydride, and the cresalol is purified by repeated crystallisations from alcohol.

Physical and Chemical Properties.—All three isomeric cresalols are bulky, white crystalline powders, with a salol-oid odor. They are insoluble in water, readily soluble in alcohol and in ether, and slightly taken up by oils. Ortho-cresalol melts at 35° C., meta-cresalol at 74° C., and para-cresalol at 39° C.

Medicinal Uses.—The employment of these "esters" in medicine depends upon the readiness with which they are split up in the organism into their components, cresol and salicylic acid, thus exerting a powerful and searching antiseptic action. As the cresols are more powerful antiseptics than carbolic acid, and at the same time are less poisonous and more mild in their physiological effects (Frænkel), the cresalols would seem fitted to play an important role in intestinal antisepsis. Nencki recommends the para form for that purpose, believing it to be superior to and safer than salol. The cresalols may be usefully given in articular rheumatism and vesical catarrh, in daily doses of 1 to 2 drachms in divided portions (Sahli).

The antiseptic properties of the compounds have also been utilized externally. The experiments of Widmer showed that for this purpose the meta variety is most suitable, since, used as a dusting powder, it does not "ball," its melting point being some distance above the body temperature. Poisoning symptoms were not noticed with the compound, while it seemed to lessen the secretion of wounds more than iodoform, besides being odorless.

ALLIED COMPOUNDS.

Xylenol-salols, $C_6H_4(OH)COOC_6H_3(CH_3)_2$. The ortho-, meta- and para-xylenol salicylates have recently been prepared and recommended for introduction into medicine, particularly for internal disinfection. They are similar in their properties to salol, neutral, without much taste or odor,

soluble in alcohol and ether, and split up into their components in alkaline liquids. Hitherto no therapeutical reports have appeared.

CRESOLS.

$$C_6H_4 \begin{cases} CH_3. \\ OH. \end{cases}$$

The cresols occupy the second place in the homologous series of univalent phenols. Three isomerides exist: ortho-, meta-, and para-cresol.

Preparation.—By fractional distillation of coal-tar oil, a mixture of the three isomeric cresols, containing about 40 per cent. meta-cresol, 35 per cent. ortho-cresol, and 25 per cent. para-cresol, is obtained in the fraction boiling between 190° and 210° C. after removal of the hydrocarbons by the treatment with alkalies. This constitutes the cressylic acid or so-called 100 per cent. carbolic acid of commerce. Owing to the close agreement of the three cresols in physical and chemical properties the isolation of any one isomeride from this mixture is attered with great difficulties and expense. The pure isomerides may be prepared from the corresponding ortho-, meta-, and para-toluidines by the action of nitrous acid, or from the toluene-sulphonic acids by fusion with potash.

Physical and Chemical Properties.—Ortho-cresol melts at 31° C. and boils at 188° C.; in a melted condition at 20° C. its specific gravity is 1.05 and it dissolves to the extent of 2.7 per cent. in water. Meta-cresol is a thick liquid, boiling at 201° C., but not solidifying above —80° C.; specific gravity at 20° C. 1.028, solubility in water 1.7 per cent. Para-cresol is a crystalline solid, melting at 36° C. and boiling at 198°; specific gravity at 20° C. 1.038, solubility in water 2 per cent. All the cresols possess a phenoloid odor, give a blue coloration with ferric chloride, and resemble ordinary phenol in chemical behavior. They have a strong tendency to remain in liquid condition, especially in mixtures, and their solubility in water is considerably affected by the presence of traces of hydrocarbons.

Medicinal Uses.—It was early discovered that the cresols possessed wonderful antiseptic properties, while at the same time far less poisonous to the animal organism than carbolic acid or phenol (Frænkel). Metacresol has a stronger antiseptic action than either of its isomerides and resembles creosote in its action (Delplanque). Paracresol is next in order, and orthocresol is distinctly weaker. A serious hindrance to the employment of their germicidal activity existed, however, in the insolubility of the compounds, and for this reason they found no application for a considerable time. During the past few years attention has again been directed to the solution of the cresols in such a way as to make them available as antiseptics and disinfectants, and a number of preparations have recently been brought under the notice of the medical profession, consisting practically of solutions of the cresols. The more important are described below, as far as possible in chronological order.

DERIVATIVES AND ALLIED COMPOUNDS.

Creolin.—This was the first form in which the cresols were presented in a liquid condition for use in medicine. It is a dark-brown alkaline liquid, which forms a more or less turbid milky mixture or emulsion with water, having the characteristic odor of the preparation. With chloroform, ether, and absolute alcohol it mixes in all proportions.

Being relatively non-poisonous,—considerable quantities having been taken without fatal issue,—and free from caustic or even irritating properties, creolin has been largely adopted in surgery as an antiseptic. Its powerful germicidal and deodorant properties were established in the laboratory bacteriologically (v. Esmarch, Eisenberg, Frœhner, Haenle, Washbourn and others), and practically in surgical practice by a very large number of authorities. The literature refers to its use externally in every department of antiseptic surgery with good results, and to its administration internally in gastric fermentation, dysentery, typhoid and the like, against phthisis (Neudorfer, Blake), leucorrhœa, gonorrhœa, vesical catarrh (Kortuem).

Quite recently creolin has done good service in acute

dysentery of a typhoid character, in colitis and entero-colitis (Watson), being applied in the form of an enema containing 5 per mille of the remedy. All the cases promptly recovered. Also recommended against epidemic influenza (Rabener).

Creolin is employed pure, in solution (1 to 2 per cent.), in ointment form with lanolin (*Lano-creolin*), as a dusting powder, gauze and surgical soap (all 10 per cent.). Internally it is administered in capsules containing 5 minims each.

Lysol.—This preparation is made by dissolving in fat, and subsequently saponifying with the addition of alcohol, the fraction of tar oil which boils between 190° and 200° C.; it is a brown oily-looking, clear liquid, with a feebly, aromatic, creosote-like odor. Described as containing 50 per cent. of cresols; miscible with water, forming a clear, saponaceous, frothing liquid; also with alcohol, petroleum spirit or benzin, chloroform, carbon bisulphide and glycerin.

As the chief advantage of lysol its solubility in water is claimed; this renders it specially suitable for the immersion of instruments, since they can be taken out with ease as required. The saponaceous character of the solutions is also advantageous in many cases—rendering a special surgical soap unnecessary—but for the handling of small instruments or the tying of fine threads the hands and instruments must be dried with a sterilized towel.

Experiment has shown lysol to be five times stronger than carbolic acid, and eight times less poisonous (Cramer, Wehmer). It does not attack the operator's hands, but renders the skin soft and supple (Haenle). Used and recommended in gynæcology and general surgery (Cramer, Wehmer, Michelsen, Haenle, Pée, VonderGoltz), in skin diseases (Unna), especially in lupus (Leslie Phillips), and in veterinary practice (Straube).

Sapocarbol, Kresapol and *Phenolin* are solutions of crude cresols in soap.

Pixol and *Resol* are similar preparations made with wood-tar.

Saprol is a coal-tar disinfectant, consisting of mixtures of crude cresols and hydrocarbons, and said to contain 40 per cent. cresols, but which has the disadvantage that it does not

properly mix with water and, moreover, contains pyridine bases which possess a toxic character.

Izal contains varying quantities of cresols and hydrocarbons mixed with water and having glue as an emulsifying agent.

Solveol and *Solutol.*—The slipperiness which the saponaceous solutions of the cresols give to the hands and instruments has been already referred to as sometimes inconvenient. Researches recently carried forward, with the view of finding other means of preparing neutral aqueous solutions, showed that the salicylates, all salts of oxybenzenecarboxylic acids, of oxybenzenesulphonic acids, of benzo-benzoic acid, and of benzenesulphonic acid, as also the similar derivatives of naphtalene, possessed the property of dissolving the cresols. Solutol is such a solution of sodium-cresol in excess of cresol, and solveol a solution of cresol in creosotate of sodium. Bacteriological experiments with the solutions indicated that they were suitable for application in surgery as dilute solutions (0.5 per cent.), said to be approximately as poisonous as those of pure carbolic acid. Preferable to acid solutions as they do not attack metal.

Kresin, a light, clear, brown liquid, containing 25 per cent. cresols brought into solution with the acid of sodium cresoxyacetate. The solvent was employed under the belief that it increased the antiseptic properties of the preparation, but this was found not to be the case.

Paracresol.—Early in the year 1892 patent rights were sought for a disinfectant introduced in Germany under this name, to which the formula $C_6H_4 \begin{cases} CH_3\ (1) \\ OH\ (+) \end{cases}$ was ascribed. It was said to give with water in every proportion a pure, neutral, non-caustic, almost odorless solution, similar to that of carbolic acid, but more active and safer; from these characteristics it is evident that the substance was not the unmixed chemical compound known to the chemist as paracresol (*v. supra*). Recommended in aqueous solution with glycerin for applying to the skin when peeling in various infectious diseases, for the use of midwives as a preventive of puerperal fever, etc.

Kresolum purum liquefactum.—A preparation of pure crystallized ortho-cresol, liquefied in the same manner as crystallized carbolic acid by the addition of water, corresponding to the formula $C_6H_4(CH_3)OH + H_2O$. An aqueous 2½ per cent. solution can be easily prepared; but it must be remembered that ortho-cresol is regarded as the least active of the three isomerides.

Trikresol.—A mixture of the three cresols in their natural proportions, carefully purified from all impurities, and forming a colorless oil, specific gravity 1,045, soluble to the extent of 2½ per cent. in water, and giving clear neutral solutions. Recommended as a substitute for carbolic acid solutions, 1 per cent. trikresol solution being equal in disinfectant value to 3 per cent. carbolic acid solution (Frænkel, Gruber). Does not attack instruments, nor make the hands numb and slippery like carbolic acid and soap preparations.

Phenosalyl is a mixture of carbolic, salicylic and benzoic acids dissolved in lactic acid, with or without the addition of glycerin, introduced as a surgical antiseptic by de Christmas. A clear syrup, dissolving readily in warm water, alcohol and ether, and to the extent of 7 per cent. in cold water. Its antiseptic power is considerably superior to carbolic acid and its toxicity much less (Cornil, Duloroy). Employed in 1 and 2 per cent. aqueous solutions for disinfection of hands and instruments and for irrigations. In major operations and confinements the absence of any corrosive action renders it especially useful, the mucous membrane remaining smooth and slippery (Fraipont). Possesses a specific action on inflamed mucous membrane and a remedial action in eczematous impetigo and endometritis (Roskam). 1 per cent. ointment successfully employed in blepharoadenitis, and 0.2 to 0.4 per cent aqueous solution as an eye lotion in conjunctivitis (Berger).

Sanatol is a solution of crude cresols in sulphuric acid.

Antinonnin is a preparation of *ortho-dinitro-cresol-potassium*, $C_6H_2(NO_2)_2(CH_3)OK$, brought into commerce in form of a paste with soap on account of the explosive properties of the dry compound. It is employed in 1 per mille solution for the destruction of insects of all kinds and of fungi, having

obtained its name from its use against the nun-moth, for some years the pest of the Bavarian forests. Its general use as a disinfectant is limited by its intensive yellow-staining properties, which even subsequent treatment with potassium sulphide solution cannot perfectly remove.

Benzoyl-para-cresol, or *paracresol benzoate*, $C_6H_5COOC_6H_4(CH_3)$, prepared by the action of benzoic acid on paracresol in the presence of phosphorus oxychloride. Crystallizes from alcohol in prisms with pleasant etheral odor. Melts at 70 to 71° C. Insoluble in water, easily soluble in ether, chloroform and hot alcohol. A very powerful antiseptic (Pétit).

Other cresol salts await the attention of the physiologist and therapeutist, among which are various *Cresol cresotates*, such as *m*-cresol *o*-cresotate (melting point 57° C.), *p*-cresol *p*-cresotate (melting point 75° C.), and certain *Phenol cresotates*, as phenol *m*-cresotate (melting point 47° C.), and phenol *p*-cresotate (melting point 93° C.).

CRESOTIC ACIDS.

Synonyms : Homosalicylic Acids; Oxytoluic Acids.

$C_6H_3CH_3OHCOOH$.

These compounds, of which three are distinguished as ortho-, meta- and para-cresotic acids, are homologous with the ortho-, meta-, and para-oxybenzoic acids.

Preparation.—By the interaction of sodium and carbon dioxide and the three isomeric cresols, according to the well-known Kolbe's method of synthesising salicylic acid. They may also be prepared (1) by melting sulphonic acids of the aromatic series $C_nH_{2n-8}O_2$ with caustic alkali; (2) by melting the homologues of phenol with excess of potassium; (3) by the oxidation of their aldehydes, and (4) by the substitution of an hydroxyl group in the benzene nucleus of the toluic acids.

Physical and Chemical Properties.—These three cresotic acids crystallize in long white prismatic needles, volatile in steam. They are very difficultly soluble in cold water,

somewhat more so in hot, and readily in alcohol, ether, and chloroform. They have different melting points; viz., ortho, 160° C.; meta, 177° C.; and para, 151° C. Their aqueous solutions are colored violet by ferric chloride, and in other reactions they exhibit a resmblance to the salicylic acids.

Medicinal Uses.—The cresotic acids themselves have not been employed in medicine. Physiological experiments exhibited considerable differences between the three isomeric modifications, the ortho being a pronounced heart-poison, the meta practically inert, and the para intermediate in action, being less poisonous than salicylic acid (Demme). Since these researches, carried out in 1888, the salts of the para variety alone have been employed in medicine.

DERIVATIVES AND ALLIED COMPOUNDS.

Sodium cresotate.—A substance so called was used as an antipyretic so far back as 1876–9 (Buss, Koranyi, Gatti), but in the latter year was found to be a mixture of chiefly *p*-cresotate of sodium with variable quantities of the *o*- and *m*-compounds. The use of salts of the cresotic acids seems to have been then abandoned until the introduction of the definite

Sodium paracresotate, a finely crystalline white powder, with a bitter but not repulsive taste; soluble in 24 parts of warm water, the solution not separating on cooling. Used as an antiseptic and in the treatment of rheumatism, and considered superior to the salicylate in the absence of disturbing effects upon the digestive organs (Demme, Fraser). Extended physiological research proved that paracresotate of sodium is less poisonous than the salicylate, and that from 8 up to at least 45 grains can be taken daily for several days in succession without ill effect (Henne).

The dose recommended is about 1¼ to 1½ drachms *pro die*, in four or five divided portions; for children the daily dose is 8 to 40 grains, prescribed in mixture with syrup, brandy, or small doses of tincture of opium.

Ortho-oxydiphenylcarboxylic acid, prepared by melting 4 parts of oxy-diphenyl with 1 part caustic soda, and heating the dry residue with carbonic acid under pressure at 220° C., is said to possess antiseptic properties.

DERMATOL.

Synonym: Subgallate of Bismuth.

$C_6H_2(OH)_3CO_2Bi(OH)_2$.

The insoluble basic bismuth salt of gallic acid discovered by Heinz and Liebrecht, and introduced as an odorless substitute for iodoform.

Preparation.—A solution of 3 parts crystallized bismuth nitrate in 6 parts glacial acetic acid, and diluted with 50 parts water, is mixed with constant stirring with a warm solution of 1 part gallic acid in 50 parts water. The yellow precipitate is washed free of nitric acid, and then dried on porous plates.

Physical and Chemical Properties.—A saffron-yellow powder resembling iodoform in appearance, but odorless and almost tasteless. Insoluble in water, as well as in alcohol and ether (absence of free gallic acid). Dissolves in caustic soda solution without separation of bismuth hydroxide (distinction from other bismuth salts). The powder is not hygroscopic and does not "ball," and is indifferent to light and heat, being sterilized at 100° C.

Medicinal Uses.—As a substitute for iodoform it has the advantages of freedom from odor and from toxic properties, whilst the combination of the astringent and drying action of bismuth salts, and the reducing action of gallic acid give it specific virtues as a vulnerary (Heinz). The antiseptic action of dermatol, when in direct contact with bacteria, has been amply demonstrated, but its kolyseptic or restraining influence on bacterial development is principally due to the desiccative properties of the preparation (Bluhm, Powers, Sackur, Stone).

It is employed as a dusting powder either alone or mixed with starch or French chalk, as a 10 per cent. collodion emulsion, as 10 or 20 per cent. ointment, as paste and as gauze.

Excellent results have been obtained with dermatol in all branches of surgical practice, especially with fresh and non-purulent wounds. Wounds with profuse discharge or in a purulent condition require to be first thoroughly cleansed. Secretion is diminished and granulation stimulated (Dörnberger, von Rögner, Werther). Especially useful in gynæcology and

rectal plastic surgery (Glaeser, Asch, Fritsch, Gottschalk). In dermatology the remedy has gained a favorable reputation in the treatment of acute eczema, burns, ulcers, etc. (Rosenthal, Isaac), whilst dermatol dusting powder, containing 20 per cent. active ingredient, has become popular for perspiring feet, intertrigo, abrasions, and for toilet and nursery use. All authors agree as to the absence of any toxic and irritant effects, and it has been successfully employed for otological, ophthalmological and rhinological purposes (Szenes, Davidsohn, Aronsohn, Eversbusch).

Internally the administration of dermatol in doses of 8 grains three or four times a day has proved highly successful in the many forms of diarrhœa, especially where arising from ulcerous processes in the stomach and intestines. The antiseptic, astringent and hæmostatic action of gallic acid, and the desiccative action of bismuth makes it one of the best innocuous local remedies against diarrhœa in modern therapeutics (Colosanti and Dutto).

DITHIOSALICYLIC ACIDS.

Synonyms: Di-β-thiooxybenzoic Acids.

$$HO_2C(OH)C_6H_3S-SC_6H_3(OH)CO_2H.$$

Some nine isomeric substances of the composition indicated above seem to be possible, of which two have been introduced into medicine in the form of sodium salts distinguished as No. I and No. II.

Preparation.—Equal molecular weights of salicylic acid and sulphuryl chloride are heated to 120° to 150° C.; reaction takes place according to the equation

$$2\,C_6H_4\begin{matrix}OH\\COOH\end{matrix} + S_2Cl_2 = 2\,HCl + \begin{matrix}S-C_6H_3\begin{matrix}OH\\COOH\end{matrix}\\|\\S-C_6H_3\begin{matrix}COOH\\OH\end{matrix}\end{matrix}$$

Salicylic Acid. Dithiosalicylic Acid.

The product of the reaction is a yellow resinous mass. This is dissolved in water containing soda, and the acid reprecipitated by addition of hydrochloric acid. The mixture

of two acids so obtained is separated by means of their sodium salts, either by extraction of the dry salt with boiling alcohol, which only dissolves salt No. II, or by precipitation of salt No. I from the aqueous solution by addition of sodium chloride. The acids are liberated from the separated salts by addition of hydrochloric acid.

Physical and Chemical Properties. — Dithiosalicylic acids are described as forming pale yellow powders.

Medicinal Uses.—The acids themselves do not seem to have been at all employed in medicine, but only the various salts.

Sodium Dithiosalicylate No. 1 was the more recently brought under notice as a powerful antiseptic. Added to cultures of the most resistant bacilli in the proportion of 15 per cent. it destroys the life of the microörganisms in from two to fifteen minutes (Hueppe). Employed externally in medicine it proved successful in a severe case of ozæna (Rosenbach). Chiefly, however, the substance has found favor in veterinary practice, being applied in 2½ to 5 per cent. solutions (as lotions or compresses) in the treatment of foot and mouth disease. Strikingly beneficial results are reported (Renner and others), and the substance seems worthy of further trial.

Sodium Dithiosalicylate No. II was first tried in medicine by Lindenborn. It occurs as a greyish-white powder, very hygroscopic and entirely soluble in water. On the addition of acid a precipitate of yellow viscid drops is produced consisting of dithiosalicylic acid. A 20 per cent. solution destroys the spores of anthrax (one of the forms of bacilli most resistant to germicides) in about forty-five minutes (Hueppe), and other experiments showed that the salt is superior in antiseptic activity to salicylate of soda. In rheumatic fever, in gonorrhoic rheumatism and similar cases, it proved an effective remedy (Hueppe, Lindenborn), reducing the febrile temperature, removing pain and bringing about a reduction of local swelling. The dosage adopted was 3 grains twice a day in slight cases, or more frequently when the symptoms were more severe, with intervals of an hour between each dose. Tinnitus and nausea were not observed, and sweat-

ing occurred only when more than 12 grains was taken in the course of the day.

Dithion consists of the mixed unseparated sodium salts of the two dithiosalicylic acids. Largely employed in veterinary practice in 5 per cent. solution for irrigation of wounds, as dusting powder, and as a 10 per cent. salve in wounds and bruises resulting from pressure of harness, and in erysipelas, cancroid and strangles (Hoffmann). An excellent prophylactic in foot and mouth disease, 6 to 14 drachms per head of cattle, mixed with the food (Renner, Wirth, Ammerschlaeger).

Lithium Dithiosalicylate was also prepared for use in rheumatic affections, and gave good results in a few cases of arthritis and gout (Lindenborn, Frank).

Thioform is the basic bismuth salt of dithiosalicylic acid. It is a voluminous insoluble yellowish powder, without odor and with strong antiseptic properties, recommended as an odorless and non-poisonous substitute for iodoform. It contains 41.5 per cent. dithiosalicylic acid, which is gradually dissolved out by the serous fluid exuding from wounds, thus exerting a penetrating antiseptic action, whilst the bismuth residue acts as a drying agent and protective layer (Baum). A mild desiccative vulnerary free from any toxic effects, which has an almost specific action in burns and ulcers, promoting healthy granulation and a rapid healing of wounds of great extent (Schmidt, Hampel). Rapidly healed extensive gangrene where iodoform was ineffectual (Lampé). Employed as a dusting powder, and also as a 10 per cent. thioform gelatine, in which form it was especially useful in moist eczema (Hübscher). All authors agree as to the absence of any irritant effect on the skin. Administered also internally as an intestinal antiseptic, in doses of 5 grains three times daily, with success, and without the appearance of any evil effects (Schmidt). The remedy has also been employed in veterinary practice with like success, both as a dressing for wounded and ulcerous surfaces and internally in chronic catarrh of the stomach and intestines (Hoffmann, Jelkmann).

DERIVATIVES AND ALLIED COMPOUNDS.

Tetrathiodichlorsalicylic acid is prepared analogous to dithiosalicylic acid by heating salicylic acid with double its mole-

cular equivalent of sulphuryl chloride. It is a reddish-yellow resinous mass, the sodium salt of which is soluble in water and possesses a marked antiseptic action.

Thiosalicylic Acid, $C_6H_4(SH)COOH$, is prepared from anthranilic or amidobenzoic acid by the successive action of nitrous acid and sulphuretted hydrogen. It is adapted for antiseptic use in the same way as salicylic acid and its other sulphur-derivatives, and by its oxidation yields a new source for the preparation of **Saccharin**, (q. v.).

Potassium Dithiocarbonate, K_2COS_2, prepared by the action of carbon bisulphide on caustic potash solution when boiling. It forms an orange-red crystalline salt, which rapidly deliquesces, is easily soluble in water, but less so in alcohol. Owing to its contents of sulphur, it has been employed in 5 per cent ointments and solutions in various skin diseases, but with no advantage over ichthyol (Tommesole and Vicini).

Sulpho-salicylic acid, $C_6H_3SO_3H(OH)COOH$, occurs as white crystals, readily soluble in water and in alcohol. It is formed by the action of sulphuric anhydride on salicylic acid and has been recommended as a substitute for salicylate of sodium in articular rheumatism.

Salicyl-sulphuric acid, as it is also termed, is a remarkably delicate and precise test for proteids of all classes, albumens, globulins, fibrin, proteoses and peptones. A dense bulky white precipitate is formed, which is not redissolved on boiling unless the body were an albumose or peptone, and then it appears on cooling; the precipitate is readily soluble in dilute alkali. The reagent detects 1 part of white of egg in 12500 parts of water (Mac William). In using it for urine (*ibid.* and Roch) the acidity of the latter should be ensured; the tube is shaken quickly and examined at once. The occurrence of an opalescence or cloudiness immediately or within 2 or 3 seconds is an indication of proteids. If the precipitate or opalescence be caused by ordinary albumen or globulin, commonly present in albuminous urine, it does not disappear on heating, but on the other hand becomes markedly flocculent. But if due to the presence of albumoses or peptones it clears up on heating (before the boiling point is reached) and appears when the tube cools.

DIURETIN.

Synonym : Sodio-Theobromine Salicylate.

$C_7H_7NaN_4O_2.C_6H_4OHCOONa.$

A definite double compound of sodium theobromine and sodium salicylate.

Preparation.—By the interaction of molecular weights of sodio-theobromine and sodium salicylate in aqueous solution, and evaporation to dryness.

Physical and Chemical Properties.—A white amorphous powder, with a slight alkaline saline taste, soluble in less than half its weight of water when warmed, the solution remaining perfect on cooling. Theoretically it should contain 49.7 per cent. of theobromine and 38.1 per cent. of salicylic acid.

Further characteristics of pure diuretin are that it burns away without residue, and dissolves readily and completely in soda solution. The aqueous solution is strongly alkaline and is rendered turbid even by such weak acids as carbonic anhydride, and it is therefore necessary that the preparation be kept in powder form and away from the air.

The preparation is estimated according to the amount of theobromine it contains. The aqueous solution is acidified, then made alkaline with ammonia, and the separated theobromine collected on a filter, washed and dried. By this method a pure compound should yield at least 46.5 per cent. of alkaloid.

The salicylic acid may be determined by shaking out the acidified filtrate and washings from the theobromine with ether, separating the extract, evaporating off the solvent and weighing the residue. It should not be more than 38.5 per cent.

Caffeine is detected by dissolving the precipitated alkaloid by addition of potash, shaking out the solution with chloroform, and evaporating off the menstruum; residue amounting to more than ½ per cent. of the alkaloid taken is made up to its actual percentage by the more soluble caffeine.

Medicinal Uses.—Like caffeine and theobromine, diuretin has a marked diuretic action; compared with the

former it is superior in having no serious or dangerous cardiac action, while it has the advantage over the pure alkaloid of being freely soluble. In doses of from 45 to 90 grains *pro die* in divided portions it acts as a pure diuretic, without effect upon the heart (Gram, Schroeder). Later observers, with a few exceptions, note however that diuretin strengthens and regulates the heart's action, as is shown by an increase of blood pressure and by sphygmographic tracings (Pfeffer, Babcock, Kress, Hoffmann, Geissler). Diuretin has been successfully employed in dropsy of both cardiac and renal origin, in hepatic cirrhosis, and in various diseases of the heart and kidneys accompanied by œdema (above named authors and Pierez). Is most efficient in chronic nephritis and without any accumulative or habitudinal action (Demme, Frank).

The volume of urine excreted in the twenty-four hours increases during the administration of diuretin three or four-fold, and even more in some cases, without any prolonged after-effect or by-symptoms; exudations of a non-inflammatory character are rapidly absorbed (Masius); slight diarrhœa is not infrequent (Pfeffer, Kress). Given to healthy persons no increase in the quantity of urine has been observed (Hoffmann, Pfeffer). Possesses a very disturbing action on the nervous system of some patients (Höhns).

The daily dose of diuretin is 60 to 105 grains, in divided portions of 15 grains. Being readily soluble in warm water it is best given in the form of mixture, either simply dissolved in water or with the addition of flavoring agents, such as peppermint oil or water, etc. Addition of acid and of acid vegetable juices should be strictly avoided, as they throw out the theobromine, which falls to the bottom of the bottle as a thick white sediment. It may also be prescribed in pill form, but not well in powders, as it absorbs carbonic acid from the air.

DERIVATIVES AND ALLIED COMPOUNDS.

Uropherin, or *Lithium-Diuretin*, is the corresponding theobromine-lithium-lithium salicylate, perfectly analogous to diuretin, only differing in the substitution of lithium for sodium. It is a white powder, soluble in 5 parts of water.

Clinical experiments show that uropherin is more easily absorbed by the system than diuretin, and the same therapeutical effect is produced with smaller doses, 15 grains three or four times a day. The diuretic action has been excellent in acute nephritis and in cardiac dropsy, but almost failed in cirrhosis of the liver and chronic nephritis (Gram). The remedy has a direct action on the heart like diuretin, and its action is rendered thereby more regular and the pulse stronger. Bad effects have not been observed, except in idiosyncrasy against salicylic acid, and this has been met by the substitution of a uropherin benzoate for the salicylate.

Antispasmin, the double salt of narceine sodium and salicylate of sodium, is a whitish, slightly hygroscopic powder, which dissolves readily in water to a light yellow liquid. The compound has an alkaline reaction, and contains 50 per cent. narceine. It is decomposed by carbonic acid, and must therefore be kept away from air and moisture. An excellent hypnotic and sedative in painful affections, especially suitable for cramp, in tussis convulsiva, and in the whooping cough of children (Demme). Administered in doses of $\frac{1}{8}$ to $1\frac{1}{2}$ grains it is free from the bad effects of both narceine and sodium salicylate.

Caffeine-sodium benzoate, *caffeine-sodium cinnamate*, and *caffeine-sodium salicylate* have also been prepared by evaporation of the aqueous solutions of equal parts of caffeine and the respective organic sodium salts. They form white, soluble powders, which are apparently merely mixtures of the two substances, and have the therapeutical action of such.

Ethoxy-caffeine, $C_8H_9N_4O_2(OC_2H_5)$, is prepared by conversion of caffeine into its mono-bromine derivative, and boiling the latter with alcoholic potash. Colorless needles, much less soluble in water than caffeine, soluble in alcohol. It melts at 138° to 139° C. Like caffeine it gives the purple murexide reaction, but is distinguished from it by its almost complete precipitation by alkalies from its solution in 100 parts boiling water.

Ethoxy-caffeine has a similar action to caffeine on the pulse and blood-pressure, but is also narcotic (Dujardin-Beaumetz). Administered in 3 grain doses, dissolved in sodium

salicylate solution, against migraine and trigeminus neuralgia. Subcutaneous injections have an anæsthetic action (Ceola). Forms easily soluble double compounds with sodium benzoate and sodium salicylate.

Caffeine tri-iodide, or *di-iodo-caffeine hydriodide,* $C_8H_{10}N_4O_2I_2$, HI + 1½ H_2O. Dark green prisms with metallic lustre, which separate from a dilute alcoholic solution of caffeine to which hydriodic acid is added, when exposed to sunlight. Easily soluble in alcohol. In the stomach iodine is gradually split off from the compound and is easily absorbed without causing the depressing effect of the alkaline iodides. In 2 to 4 grain doses as a mild iodine preparation (Granville).

Iodocaffeine and *iodotheobromine,* prepared by leading sulphuretted hydrogen into a solution of potassium iodide and the respective alkaloids, consist of colorless crystals moderately soluble in water. Iodocaffeine is indicated in cardiac affections, where the amplitude of the diastole is to be increased, as in mitral stenosis, and relieves degenerative processes of the liver. Iodotheobromine is indicated in cases of cardiac disease, where diuresis must be increased and the cardiac systole increased, as in aortic insufficiency. Both remedies are well borne in doses of 5 to 7 grains two to six times daily in cachets (Rummo).

Caffeine-sulphonic acid, see under **Symphorol.**

ETHYL BROMIDE.

Synonyms: Brom-ethyl; Æther-bromatus; Monobrom-ethane.

C_2H_5Br.

Preparation.—Alcohol and pure concentrated sulphuric acid are mixed together, allowed to cool, placed in a retort, and powdered bromide of potassium added in small portions, keeping the mixture as cool as possible. When the reaction is complete, distillation is effected at 125° C. on a sand bath. The distillate is purified by washing with potassium carbonate and water, subsequent removal of water by chloride of calcium, admixture of 10 per cent. by weight of fresh almond or olive oil, and redistillation from a water bath.

Physical and Chemical Properties.—A colorless, limpid, inflammable liquid, with a sweet chloroformic odor and a burning taste. It boils, when pure, between 38° and 39° C.; specific gravity 1.38 to 1.39 at 15° C. Not miscible with water, but freely with alcohol, ether, chloroform and oils. Under the combined action of air and light it decomposes, becoming gradually brown and acid in reaction (free bromine and hydrobromic acid).

These impurities are detected by shaking with an equal volume of water, and testing the latter with blue litmus paper and argentic nitrate, when, if hydrobromic acid be present, the former is reddened and the latter precipitated. Traces of free bromine are evidenced by the violet color of the globules, which reach the bottom of a potassium iodide solution a little more than an inch deep, when a few drops of ethyl bromide are allowed to slowly fall into it. Shaken with an equal volume of pure concentrated sulphuric acid, no coloration should be produced after 24 hours (ethylene and amyl compounds). Of course preparations with the slightest pungent or unpleasant smell are quite unfit for use in medicine.

Medicinal Uses.—Ethyl bromide is very largely used as a general anæsthetic in minor surgery. The narcosis is produced in from ½ to 1 minute, and lasts only a few minutes unless fresh quantities be administered. Its effects are produced more rapidly than those of chloroform, while at the same time it has not the unpleasant after-effects of the latter (Szuman, Nunnely, Lewis, Langgaard, and others). An ordinary chloroform mask can be employed, being covered with thick flannel upon which the anæsthetic is poured; the mask is then fitted close to the face. In this way about 3 drachms, seldom so much as 6 drachms, is sufficient to produce the necessary degree of anæsthesia. Its use appears to require caution and watchfulness in consumptives and in patients suffering from cardiac or renal disease. Consciousness is not apparently entirely lost in every case, but the sensation of pain is largely or entirely annulled. The number of narcoses which have been carried out with ethyl bromide is very great; the latest observers (Cockburn-Smith, Ziemacki)

report very favorably upon the action of the anæsthetic in several hundreds of cases. It is advised to pour a few drops only to begin with upon the mask, and then about 2 drachms at once, so that it is saturated with the liquid. Recommended in the treatment of children when changing dressings—often a painful operation, and in operating upon goitre (Krecke).

DERIVATIVES AND ALLIED COMPOUNDS.

Ethyl chloride, C_2H_5Cl, also called *Chelen or Kelen*, is prepared by a patented process involving the direct action of hydrochloric acid upon alcohol under high pressure. It occurs as a colorless liquid, with a pleasant ethereal odor; boiling point 10° C. (50° F.); readily inflammable. The liquid is introduced into commerce in small tubes, each containing nearly 3 drachms, hermetically sealed with a capillary point. Recently it is also sold in glass tubes with a fine metallic nozzle which can be tightly screwed up. It is employed as a local anæsthetic, acting by the virtue of the intense cold produced by its rapid evaporation. When used the point of the tube is broken off, and the heat of the hand is then sufficient to expel the liquid, through the minute orifice formed, in a stream which can be directed to any desired point. The mucous membrane, *e. g.* of the gum in tooth extraction, is first dried and then rubbed with glycerin or oil; the spray is applied until the membrane becomes white, when the anæsthesia is complete. The tooth itself must be carefully protected from the action of the liquid, and the best results are obtained when the tube is held at some distance from the place to be anæsthesised. During the application the patient should breathe through the nose only (Redard).

The lowest temperature attainable by ethyl chloride is —35° C. Ethyl chloride is recommended for use in minor surgery generally, such as the treatment of ingrowing nail, the opening of abscesses, the relief of facial neuralgia, sciatica, etc. (Ferrand, Grandeclement, Scheller).

The ready inflammability of the compound and its vapor must be kept in mind, and operations performed at a good distance from gas or other flames, or by electric light. It has the advantage over some other local anæsthetics of being

without unpleasant after-effects or influence on the sensorium.

Coryl is a mixture of methyl and ethyl chlorides.

Ethyl iodide, C_2H_5I, prepared by gradually adding 10 parts iodine to a well-cooled mixture of 1 part amorphous phosphorus in 5 parts absolute alcohol, and distilling off after standing 24 hours, is a colorless liquid, boiling at 71° C. Employed as inhalation in bronchitis, dyspnœa.

Ethylene bromide, $C_2H_4Br_2$, is a faintly-brown colored liquid, with an odor resembling that of chloroform, and a sweet taste with an after-burning sensation. At 0° C. it solidifies to a snow-white crystalline mass, and its boiling point is 131° C., specific gravity 2.163 at 21° C. Insoluble in water, but miscible in all proportions with rectified spirit, and forming perfectly clear solutions with fatty oils.

In spite of their widely different physical properties, the similarity in name has led to confusion of ethylene bromide and ethyl bromide. It is important to avoid such an error since the ethylene compound is capable of producing marked poisonous effects when inhaled; several such cases are recorded in literature.

As a bromine compound not associated with a powerful basylous radical, ethylene bromide has been used in epilepsy as a substitute for patassium bromide, which, when long continued, produces poisoning symptoms. In 10 cases of epilepsy treated with ethylene bromide the attacks became less frequent, shorter and milder, sometimes degenerating into mere muscular twitchings without unconsciousness (Donath). The dose of the compound adopted was 6 to 12 drops in emulsion, in spirituous solution (equal parts, the dose being stirred up in a glass of milk), or in capsules with ol. amydal. dulc. For subcutaneous injection solutions in oil are recommended.

EUGENOL.

$C_3H_5.C_6H_3(OH)(OCH_3)$.

Nature and Source.—A phenol, found in many essential oils, especially those of cloves, pimento, cinnamon, sassafras, bay.

Properties and Uses.—An aromatic, oily liquid, boiling at 246° C. On exposure to the air it turns brown. Readily soluble in alcohol, but only very sparingly so in water; it forms compounds of definite character with caustic alkalies.

Eugenol is a powerful antiseptic, regarded as superior in this respect to phenol. Having an agreeable odor it is well suited for use in dental surgery. Has also been recommended as a febrifuge and as a remedy in tuberculosis, but not much employed.

Dose.—45 minims *pro die*, dissolved in spirit and diluted with water.

Several derivatives of eugenol have recently been brought under the notice of the medical world, which may be briefly mentioned here:

Benzoyl-eugenol, $C_3H_5.C_6H_3(OCH_3)CO_2C_6H_5$, occurs in neutral acicular crystals, which melt at 70.5° C., are free from color and odor, and have a feebly bitter taste. Scarcely taken up by water, but freely by hot alcohol, by chloroform, ether and acetone.

Cinnamyl-eugenol, $C_3H_5.C_6H_3(OCH_3)CO_2(CH)_2C_6H_5$, forms neutral, lustrous needles, free from color, odor and taste; m. p. 90° to 91° C. Scarcely soluble in water, but readily in the other solvents named above.

These compounds are being clinically tried in the treatment of tuberculous affections.

Iodo-eugenol, obtained by treatment of eugenol in alkaline solution with iodine, is a yellowish insoluble powder, without odor, and possessing antiseptic properties.

Eugenol-acetamide, $C_3H_5.C_6H_3(OCH_3)OCH_2CONH_2$, is prepared by the interaction of eugenol-sodium and monochloracetic acid, and the subsequent conversion of the eugenol-acetic acid formed into the amide by heating with ammonia; shiny crystals, crystallizing from water and alcohol, and melting at 110° C. Possesses a local anæsthetic action, and has been recommended as a substitute for cocaine, but further clinical results are wanting up to the present time.

EUPHORIN.

Synonym : PHENYL-URETHANE.

$C_6H_5NHCOOC_2H_5$.

A crystalline compound structurally allied both to carbaminic acid and to acetanilide.

Preparation.—By the interaction of aniline and monochloroformic ethyl ester.

Physical and Chemical Properties.—A white crystalline powder, with a faint aromatic odor, and slight after-taste of cloves. Practically insoluble in water, readily soluble in alcohol, or in mixtures of water and alcohol, such as wines. Melting point 51° C.

Medicinal Uses.—First recommended in 1890 as an antipyretic and antirheumatic, acting as an energetic and safe antifebrile, improving the general well-being, relieving the pain, and reducing the joint swelling in rheumatism without producing collapse and cyanosis (Giacosa, Sansoni, Adler). The analgesic action was also prompt in neuralgias, sciatica, and the like. In a few cases of advanced tuberculosis of the lungs with high evening temperature, the compound was administered with very good success, the temperature falling from 1.4° to 2° C. in half an hour after the administration of the powders (Adler). All the observers speak well of the freedom of the action of euphorin from unpleasant by- or after-effects. Although its antithermic action is powerful and free from ill-effects it is somewhat unreliable, and as a sedative antirheumatic it is surpassed by other preparations (Köster).

The antiseptic virtues of the preparation have also been made use of in the treatment of ulcers, chronic ophthalmia, skin diseases, and the like. It reduces the secretion of wounds, and the slight amount which persists assumes a serious character. On the other hand, no disturbances of any kind were observed. The most encouraging results were also obtained in general surgery (Oliva). Applied to venereal ulcers deodoration was affected in a few hours, and without the slightest pain the ulcers cleaned up and formed healthy granulations less irritable than those produced by iodoform.

Euphorin prevents the spread of the venereal ulcer from the wound to the inguinal glands (Peroni, Bovero). Excellent results have been obtained by its employment in gynæcology, and especially in the treatment of erosions of the urethra, where its slight astringent action and absence of any irritant effect has been invaluable (Pintor).

As an antipyretic the remedy is given in doses of 8 grains, and against rheumatism 6 grains three, four or five times a day, in wafers, dissolved in wine, or suspended in water. Euphorin cannot be prescribed in powders with antipyrine, as a liquid is formed when the two substances are rubbed together (Suchanek). Externally the substance itself is applied as a dusting powder, as ointment (with lanolin), and as superfatted medicinal soap.

EUROPHEN.

Synonym: Di-isobutylortho-cresol iodide.

$$2\left(\begin{matrix}C_4H_9\\CH_3\end{matrix}\right\rangle C_6H_3O\Big)HI.$$

A recent addition to the class of iodoform substitutes, allied to aristol.

Preparation.—By the interaction of isobutyl alcohol and ortho-cresol in the presence of zinc chloride at a high temperature isobutyl-ortho-cresol is formed. This dissolved in dilute alkali and precipitated with a solution of iodine in potassium iodide, yields the europhen, which is washed and dried in the dark. Recently europhen is said to be also produced by the aid of electrolysis.

Physical and Chemical Properties.—An amorphous yellow powder, of peculiar aromatic odor, reminding somewhat of saffron; insoluble in water and glycerin, readily soluble in alcohol (up to about 30 per cent.), ether, chloroform and fatty oils (up to 25 per cent.); as with aristol the solutions must be prepared in the cold. In contact with water or aqueous liquid (wound secretion) small quantities of iodine seem to be given off that are again taken up, so that

aqueous solutions always yield a slight precipitate with silver nitrate (Goldmann). Mixed with any fat and starch it is also decomposed, but in ointment form alone is quite stable. It yields iodine to metallic oxides and mercury salts. Europhen is five times as bulky as iodoform. It must be preserved in a dry place and protected from the access of light. Between the fingers it feels resinous, and adheres to the skin and mucous membrane like aristol and much more readily than iodoform. It is decomposed into its constituents by boiling caustic potosh solution.

Europhen, like aristol, may be prepared in a purer condition (free from any trace of iodine which is formed in drying it) by dissolving in alcohol and reprecipitating with water. The product so formed is of paler color and absolutely free from iodine; on the other hand, it is quite inert, having no effect whatever upon the growth and development of bacteria (Goldmann).

When heated Europhen "runs together" at about 70° C., gradually liquifying as the temperature rises, until at about 110° C. it forms a clear brown liquid. The ash amounts to 0.15 per cent.

Medicinal Uses.—Europhen exerts a more or less marked kolyseptic action upon micro-organic growth, probably by virtue of the free iodine which is set free in the nascent state when the compound comes in contact with aqueous liquids. It is undoubtedly equal in this respect to iodoform (Siebel), while the advantages are claimed for it that it is non-poisonous, odorless and specifically lighter. The use of europhen is indicated in all cases where hitherto iodoform has been employed (Eichhoff, Petersen, Loewenstein, Vulpius, Nolda, Petersen, Gibs, Shoemaker), and it has been applied in nasal diseases, syphilis, ulcus cruris, lupus and burns (Siebel, Kopp, Chappel). It is said to have a good effect in syphilis when subcutaneously injected, although this has been contradicted by Eichhoff. Europhen has proved very effective in the treatment of lepra tuberosa (Goldschmidt). On account of its inodorousness and high antiseptic value specially indicated for erosions of the penis and vulva, and fissures of the anus and balanitis (Oefelin and Neuberger).

For external use europhen is dusted on in powder, or applied as a 5 to 10 per cent. ointment or plaster-mull, with lanolin. Metallic oxides and mercurials must not be prescribed with it, nor the zinc starch paste, so much used in dermatology. For subcutaneous injection a 3 to 10 per cent. solution in olive oil is applied.

EXALGINE.

Synonym: METHYL-ACETANILIDE.

$C_6H_5N(CH_3)CH_3CO.$

A crystalline compound allied to acetanilde, first described by A. W. von Hofmann in 1874.

Preparation.—By warming together monomethylaniline and acetyl chloride. The reaction when once started takes place violently, and is represented as under:—

$$2\ C_6H_5NHCH_3 + CH_3COCl = C_6H_5N(CH_3)CH_3CO +$$

Monomethylaniline Acetyl chloride

$$C_6H_5NHCH_3Cl.$$

Monomethylaniline hydrochloride.

The monomethylacetanilide is obtained by dissolving the mass in boiling water and crystallizing out. The unchanged methylaniline is recovered by distillation from excess of soda.

Physical and Chemical Properties.—Exalgine occurs in beautiful acicular needles, difficultly soluble in cold, more readily in warm water, more easily so in dilute and concentrated alcohol. It melts at 100° C., and boils between 240° and 250° C. without decomposition.

It is converted by soda incompletely, and more readily by concentrated hydrochloric acid, into monomethylaniline. Aniline and other compounds of the base are detected, if present, by the production of a violet color when solution of chlorinated lime is added to the solution of monomethylaniline in hydrochloric acid after it has been nearly neutralized by ammonia.

Acetanilide and aniline salts are also detected by the odor of isonitrile produced when the impure exalgine is heated with

alcoholic potash and chloroform. By the provision that the aqueous solution shall not be changed by silver nitrate the absence of hydrochloric acid is ensured.

Exalgine is distinguished from acetanilide, methacetine and phenacetine by treating 2 grains with 20 minims of concentrated hydrochloric acid: insoluble = phenacetine. Acetanilide dissolves, but separates again in crystals. Methacetine also dissolves, but the solution is gradually colored reddish-brown on the addition of one drop of concentrated nitric acid.

Something has been written as to the possible confusion of exalgine and strychnine, but there seems to be no more danger in this direction with exalgine than with the number of other organic compounds which crystallize in the same form.

Medicinal Uses.—Exalgine was introduced in the expectation that it would take a foremost place in materia medica as an analgesic. Experiments on animals, however, showed it to have a powerful poisonous action, and as it was employed in medical practice a series of cases were reported in which its use, especially in overdoses by error, was followed by toxic effects resembling those of carbolic acid, with delirium, dyspnœa, cyanosis, and renal disturbances (Buisson, Dyer, and Prentiss most recently). On the other hand, some observers record excellent results in neuralgias, characterize the remedy as superior to antipyrine, and without serious by-effects (Dujardin-Beaumetz, Bardet, Gardineau). Antithermic effects are not produced unless poisonous quantities be given (Fraser). Given with success in chorea in daily doses of 3 grains (Moncorvo). Its name (from ἐξ, and ἄλγος, pain) was given to indicate its chief field of usefulness.

There has been a good deal of discussion as to the dose of exalgine, which has now abated, its whole use being limited, but the balance undoubtedly lies in favor of comparatively small doses, ½ to 4 grains, not exceeding 5 grains. Sometimes prescribed in powder, occasionally in pills, but most frequently in mixtures with some form of alcohol: half a drachm of rectified spirit and one ounce of water form a permanent solution with 16 grains. Useful formulæ are:

I.	II.
℞ Exalgini ..... gr. 48	℞ Exalgini ..... gr. ii
Tr. cort. aur. ..... ℥ iss	Sp. vini gall. ..... ʒ ss
Syr. aurant. ..... ℥ i	Syr. aurant. ..... ʒ iii
Aquæ ..... ad ℥ vi	Aquæ ..... ad ℥ ii
M. 1 ach tablespoonful contains 4 grains.	M.

It is recommended in dispensing to dissolve the exalgine in slightly warm, not hot, water and add the spirit and flavoring; so made the solutions are permanent.

Aceto-ortho-toluide, $C_7H_7NHC_2H_3O$, the isomeride of exalgine, in which the methyl group is present in the benzene nucleus instead of attached to the nitrogen atom, is a colorless crystalline substance, sparingly soluble in cold water, easily in hot water, alcohol and ether, melting at 107° C. and boiling at 296° C. Like acetanilide and exalgine it is a powerful antipyretic (Barbarini). Exact reports as to therapeutical indications and dosage have not yet appeared.

FORMIC ALDEHYDE.

Synonyms : Formalin ; Formol.

$H.CHO$.

The aqueous solution of the gaseous oxidation product of methyl alcohol, corresponding to acetic aldehyde.

Preparation.—By conducting the vapors of methyl alcohol mixed with air over glowing coke or metal spirals. The condensation product consists of an aqueous solution containing formic aldehyde, unaltered methyl alcohol, and traces of formic acid. The alcohol is removed by distillation, and the solution concentrated to 40 per cent. strength.

Physical and Chemical Properties.—Absolute formic aldehyde has been liquefied at very low temperature, and boils at —21°C.; at —25°C. it has a specific gravity of 0.8153, and at —80° C. of 0.9172 (Kékulé). The 40 per cent. aqueous solution is a colorless, neutral liquid, specific gravity 1.080 to 1.088 at 18° C., rapidly diffusing vapors of a penetrating pungent odor, and miscible in all proportions with water.

In more concentrated solutions formic aldehyde has a great tendency to revert to its polymeric modification, paraformic aldehyde (*q. v.*), which is also left as a white residue on evaporation of dilute solutions, but is completely volatile at higher temperatures.

Formic aldehyde solutions reduce ammoniacal silver solution and Fehling's solution. With ammonia combination takes place with the formation of a soluble inodorous base which is left as a white solid on evaporation.

$$6\,CH_2O + 4\,NH_3 = (CH_2)_6N_4 + 6\,H_2O.$$

Formic aldehyde. Ammonia. Hexamethylenetetramine.

With aniline water formic aldehyde in dilute solution gives a milky turbidity, in more concentrated solutions crystalline precipitates with aniline, phenylhydrazine, and acid sulphites of the alkalies. It also combines readily with sulphuretted hydrogen, mercaptan, skatol, and foul-smelling ammoniacal bases, to form inodorous products. With albumen and gelatine it combines to produce peculiar insoluble compounds.

The percentage strength of formic aldehyde solutions may be determined by their specific gravity (Lüttke), and volumetrically by adding 20 c.c. normal ammonia solution to 2 c.c. formic aldehyde solution, allowing to stand several hours in a stoppered flask until totally converted into hexamethylenetetramine, then diluting and titrating back with normal sulphuric acid, using methyl orange or cochineal as indicator. 98 parts by weight of sulphuric acid equal .120 parts by weight of formic aldehyde (CH_2O). Whether the formic aldehyde is present in its simple or polymeric form can only be determined by a Raoult estimation of the molecular weight.

Medicinal Uses.—Formic aldehyde was discovered by Berlioz and Trillat in 1890 to possess very great antiseptic powers and they found that an addition of 1 to 50000 parts was sufficient to prevent the development of bacteria in meat juice. Almost simultaneously Loew recognized it as a powerful poison to the vegetable protoplasm. On these grounds it was introduced as a relatively non-poisonous antiseptic, and during the past two years has found continually

extending employment as a germicide, disinfectant and preservative, in which its deodorant properties have also been utilized.

In solutions of 1 to 20000 it kills anthrax bacilli, and in 1 per mille solutions anthrax spores after 1 hour's exposure (Stahl). Numerous bacteriological investigators (Hauser, Gegner, Aronson, Lehmann, Blum, Slater, Rideal) have shown that in germicidal power it is at least equal to corrosive sublimate, in presence of albuminoids stronger, whilst its vapors are equally active (Segall, Buchner and others) and owing to their ready diffusiveness afford a most effective means of disinfecting rooms. It is equally inimical to the moulds and parasites of plant life (Wortmann, Cohn).

As both solutions and vapors are without any deleterious effect upon tissues and most delicate objects and colors generally, formic aldehyde is especially adapted for the disinfection of clothing, bedding, furniture, toilet articles and household goods of all kinds (Lehmann). Any clinging odor is readily removed with ammonia.

As a preservative the use of formic aldehyde has been recommended for the preservation of various anatomical and zoological specimens, for which it is preferable to methyl alcohol (Schmidt, Blum). Also as a hardening agent and for the preservation of cultures of bacteria and gelatine, etc., in any stage of development (Hauser, Hermann, Merkel). Owing to the extraordinary properties of formic aldehyde in combining with gelatines and albuminoid substances, the natural appearance and even colors of preparations are permanently retained. In the absence of toxic properties formic aldehyde has also been recommended as a preservative for foods, wine, beer, etc. (Jablin-Gonnet).

In surgical operations formic aldehyde is most useful for cleansing and sterilizing materials and instruments, as well as the hands (all authors). It is not suitable for the antiseptic treatment of wounds (Berlioz). Its local action in concentrated solution on the animal skin is most peculiar, rendering it necrotic without any appearance of inflammation (Gegner), which property may be utilized for the removal of warts and superfluous growths, in chronic skin diseases, as

psoriasis, lupus, etc., and in ulcerous affection by the careful application of 2 per cent. solutions. Although the mucous membrane is still more sensitive to the remedy, it can be employed as a gargle in less than half per cent. solution (Gegner), and inhalations have proved beneficial in chronic catarrh (Stavenhagen). The addition of 1 part per 2000 is recommended for the preservation of collyria, as its irritant effect on the eyes is minimal, whilst atropine and eserine solutions may be kept sterilized for a month by this means (Valude). Suggested as a spray in diphtheria in 1 or 2 per cent. solution (Alleger).

For ordinary purposes of disinfection a 1 per cent. solution is sufficient, but the stronger solution should be used for standing in the sick-room to purify the air, or elsewhere as deodorant. For hardening preparations for microscopic purposes a 4 per cent. solution is employed, and for use in museums 10 per cent. solutions are recommended.

DERIVATIVES AND ALLIED COMPOUNDS.

Para-Formic Aldehyde, $(CH_2O)_3$, the polymerized form of formic aldehyde, into which it is readily converted when heated or strongly concentrated, is a white crystalline powder, melting at 171° C., soluble in water and giving solutions possessing most of the characteristics of ordinary formic aldehyde, owing to its gradual reversion to the latter state. When volatilized it also reverts to the simpler condition in vapor form, but is redeposited as a sublimate in the polymerised condition. Surgical dressings and bandages impregnated with paraformic aldehyde are prepared in this way. Its internal administration depends upon its antiseptic properties, in which it is said to excel aristol, salol, naphtalene and betanaphtol (Aronson). 75 grains were taken without bad effects and digestive action is not interfered with. Administered successfully in doses of 8 to 15 grains in the cholera nostras of children.

Formalith.—A preparation of infusorial earth saturated with 50 per cent. Formalin, affording a convenient means for the application of formic aldehyde for disinfectant and sterilization purposes.

GALLACETOPHENONE.

$CH_3COC_6H_2(OH)_3$.

A derivative of pyrogallol containing an acetyl group as well as three hydroxyl groups. Introduced primarily under the less intelligible name "Gallacotophenone."

Physical and Chemical Properties.—A pale yellow powder, crystallizing from hot water, in which, as also in alcohol and in ether, it is readily soluble. Cold water takes up only 1.8 per mille, but by the addition of 30 per cent. of sodium acetate a 4 per cent. aqueous solution can be made: glycerin dissolves it in every proportion.

Medicinal Uses.—Recommended instead of pyrogallol, which often gives rise to poisoning symptoms, in the treatment of psoriasis; gallacetophenone has less powerful reducing properties than pyrogallol, and the further advantage that it does not soil the linen with which it comes in contact.

Gallacetophenone, having been proved harmless to animals, was tried in a few cases of psoriasis in human beings with encouraging results (Rosenthal). A good effect is observable within 12 hours after the application (Rekowski). Also tried successfully in several cases of eczema (Goldenberg).

ALLIED COMPOUNDS.

Gallanol, or *Gallic acid anilide*, $C_6H_2(OH)_3CONHC_6H_5 + 2\,H_2O$. Colorless crystals of slightly bitter taste, insoluble in cold water, soluble in hot water, alcohol and ether, insoluble in benzene and chloroform. The pure anilide melts at 205° C. Gallanol is recommended as a substitute for chrysophanic acid and pyrygallol in various skin diseases, on account of its freedom from toxic and unpleasant properties. In acute and chronic eczema it has been successfully employed in 2 to 10 per cent. ointments, in moist eczema as a dusting powder mixed with French chalk, and in psoriasis suspended in chloroform or traumaticine (Cazeneuve and Rollet). Its action is less rapid than that of chrysophanic acid, but causes no reddening or discoloration of the skin, is odorless, does not stain linen, and may be used freely (Barendt). Its antiparasitic action has also been manifested in

the successful treatment of mycosis, favus, trichophytis, and in prurigo (Nicolas, Gonon, Hubscher).

Gallobromol, see under **Bromol.**

GUAIACOL.

Synonym: Methylpyrocatechol.

$C_6H_4OHOCH_3$.

In medicine guaiacol is understood as the liquid compound which constitutes from 60 to 90 per cent. of beechwood tar creosote, chemically pure guaiacol only being prescribed when guaiacol "cryst" is ordered (*v. infra.*).

Preparation.—By fractional distillation of beechwood-tar creosote, the fraction passing over between 200° and 205° C. being collected. This is freed from acid compounds by agitation with dilute ammonia, and fractionated again. The lower boiling fraction is dissolved in an equal volume of ether, and decomposed with a concentrated alcoholic solution of potash, potassium-guaiacol being formed. This is washed with ether, crystallized from alcohol, and the guaiacol set free by dilute sulphuric acid. Another method involves precipitation of creosote with barium hydrate($Ba[HO]_2$), and separation of the compounds formed, advantage being taken of their differing degrees of solubility.

The purification of guaiacol—even the "guaiacol absolut." of commerce contains foreign compounds, such as cresols—may be effected by repeatedly recrystallising benzoyl-guaiacol (*q. v.*), until odorless and of constant melting point. This is saponified by boiling with the quantity of alcoholic potash calculated to take up the amount of benzoic acid combined with it under a return condenser. After evaporation of the alcohol, shaking out with ether and volatilizing off the solvent, the guaiacol is obtained and is further purified from small quantities of ethyl benzoate by solution in dilute soda, filtering, setting free by sulphuric acid, washing, drying and rectifying.

Physical and Chemical Properties. — The purified guaiacol obtained by the second process described above, is a somewhat colored liquid, with an agreeable odor, a sp. gr. at 15° C. of 1.133, and boiling at 206° to 207° C. Soluble in water in the proportion of 1 to 85, in petroleum benzene 1 to 8 (Bongartz). Readily soluble in alcohol and ether.

With concentrated sulphuric acid it gives a faint yellow coloration, which is changed to cherry red by the addition of a small proportion of acetone. In alcoholic solution it gives a blue color with a trace of ferric chloride, changing to green as more of the salt is added. This reaction is characteristic.

The various guaiacols of commerce differ from the above characters in having a lower specific gravity and boiling point, and in giving more or less red color with concentrated sulphuric acid alone. They darken on exposure to air and light. Guaiacol is excreted with the urine, and also makes its appearance in the saliva and perspiration. The method of detecting it is described under **Benzosol** (*q. v.*).

The compound forms crystalline salts with the metals, an atom of these elements displacing the hydrogen of the hydroxyl group, as potassium guaiacol: $C_6H_4OCH_3OK$. The compounds are, however, unstable and decomposed by much water. It also combines to definite chemical bodies with acid radicals; some of these, which have been introduced into medicine, are described below.

Medicinal Uses.—According to Guttmann, tubercle bacilli are destroyed by blood which contains ½ per mille of creosote, while even half that proportion arrests their growth. On this statement the intensive creosote treatment of phthisis was based, which consists in commencing with a daily dose of 2 minims and increasing the amount 1 minim daily, until 15 to 18 minims are being taken *pro die* in the form of capsules; in this way an accumulation of creosote in the blood and fluids of the tissues has been believed to be attained corresponding to that pointed out by Guttmann as theoretically necessary (Sommerbrodt, Schetelig). Guaiacol was introduced as a substitute for creosote (Schueller, Sahli), being the principal ingredient of the latter and of definite chemical nature; the same dosage as that given above for creosote has

frequently produced distinctly beneficial effects in the early stages of the disease. It is preferable to creosote, as it does not disturb the stomach to the same extent (Reese).

It is interesting to note that quite recent researches indicate that the good effects of the creosote or guaiacol treatment of pulmonary tuberculosis are due neither to the kolyseptic (or development-hindering) properties of guaiacol, as some authors (including the originator of the treatment) believe, nor purely to its stomachic and tonic virtues (as others have asserted), but to the fact that it forms compounds, eliminable from the blood in a dissolved state, with the toxic albuminous by-products of the activity of the tubercle bacillus (Hoelscher and Seifert). It is to these albuminoids that the fever, night sweats, and disturbances of appetite, digestion and general well-being must be ascribed, and with their removal or conversion into inert compounds all these symptoms disappear, as seen in the action of guaiacol and the various compounds described below.

Guaiacol is administered in the above dosage in mixture with wine or brandy (best after meals), or in capsules, or combined with cod-liver oil. Also employed in the form of inhalations, 5 to 10 drops with hot water being inhaled several times a day (Schueller). Subcutaneously 3 to 15 minims have been injected in the pure state (Schetelig, Polyak, Bourget), or in 20 to 30 per cent. solution in almond oil.

Recently the endodermical application of guaiacol in tuberculosis (Sciolla, Védrine) and as an antipyretic in typhoid fever and other febrile diseases (Da Costa, Bard) has been recommended. It is applied with a brush to the previously cleansed skin and immediately covered with an impermeable dressing. Its antipyretic action is very striking, but profuse sweating and marked chills rather diminish its value (Thayer). Carter has used it externally in 13 cases and found in 114 applications the temperature reduced in 104 instances. He employed the liquid drug, rubbing from ½ to 1 drachm into the ascilla at 5 or 6 p. m. daily.

Finally guaiacol has done good service in the disinfection of tooth pulp instead of creosote (Gorgas).

Crystalline Guaiacol is prepared either from the purified

natural guaiacol from creosote by crystallization at very low temperature, or synthetically by the methylation of pyrocatechol. The chemically pure substance occurs in colorless crystalline masses, melting at 33° C., and boiling at 205° C., remaining for a long time in the liquid condition when once molten. Its specific gravity at 19° C. is 1.1365. It dissolves readily in alcohol and ether, in 50 parts water, and yields a colorless solution in sulphuric acid (Béhal, Choay, Thoms). Its therapeutical introduction is not yet general, but from the latest researches there seems no ground for the belief that the crystalline product does not have the same remedial value as the less pure forms. Crystalline guaiacol is without toxic action and produces no disturbance of the general health (Griesebach). It has been employed internally in tuberculosis in place of the liquid preparation with equally good results (Gilbert and Maurat). In its endodermical use it has met with just the same indications (Védrine).

DERIVATIVES AND ALLIED COMPOUNDS.

Guaiacol carbonate, $CO_3(C_6H_4OCH_3)_2$, the di-guaiacol ester of carbonic acid, is prepared by the action of phosgen gas (carbonyl chloride) on solution of guaiacol sodium,

$$\begin{matrix} CH_3O.C_6H_4.ONa \\ CH_3O.C_6H_4.ONa \end{matrix} + \begin{matrix} Cl \\ Cl \end{matrix}\!\!>\!CO = 2\,NaCl + CO\!<\!\begin{matrix} OC_6H_4OCH_3 \\ OC_6H_4OCH_3 \end{matrix}$$

Guaiacol sodium salt. Phosgen gas. Guaiacol carbonate.

and recrystallization of the separating crystals from alcohol. It is a white, crystalline, neutral powder, nearly free from taste and odor, insoluble in water, sparingly soluble in cold alcohol, glycerin and oils. Melts at 78° to 84° C. Decomposed by alkalies into carbonic acid and guaiacol, of which it contains 91.5 per cent.

Like benzosol this compound is to be used as a substitute for guaiacol and creosote in the treatment of tuberculosis. In doses of 6 to 8 grains, gradually increasing to 1½ drachms *pro die*, it produces improvement of appetite and increase of nutrition, and consequently of body-weight and of resistance to the effects of the disease (Hoelscher). The preparation is well borne, as it does not irritate the mucous membrane or disturb the digestive functions, for being insoluble it passes

unaltered through the stomach, and only develops its action in the presence of alkaline intestinal juices (Seifert). The advantages of this non-irritant remedy, its freedom from odor and taste, and convenient form, have been largely recognized, and its use is considered decidedly a progressive step in the treatment of tuberculosis and particularly in pulmonary consumption. Increase of appetite, gain of strength followed by a diminution of cough, and finally the healing of the pulmonary lesions are the effects noted (Chaumier). Patients who had for a long time taken creosote and guaiacol without effect, found themselves benefitted by the guaiacol carbonate, whilst on the other hand patients who after taking the medicament had increased in weight, fell off after substituting creosote for the carbonate for a few weeks (Seifert and Hoelscher).

Creosote carbonate, or *Creosotal*, is completely analogous to the above but is prepared direct from the beechwood creosote before complete purification of the guaiacol. It is an amber-yellow oil, of honey-like consistency, with only faint odor and taste, insoluble in water, and frequently deposits crystals of guaiacol carbonate on long standing in the cold. A convenient form for the administration of creosote, owing to its absorption being free from disturbing symptoms. For children in doses from 3 minims up to 15 minims pro die and for adults in doses of 15 minims three or four times daily (Chaumier).

Guaiacol carbonic acid, or *metaoxysalicylic acid*, $C_6H_3(OH)(OCH_3)COOH + 2\ H_2O$, brought out just before guaiacol carbonate and confused with the latter, is prepared from guaiacol, in the same manner as salicylic acid from phenol, by saturating sodium-guaiacol with carbon dioxide, heating the mixture in closed vessels to 100° C., and separating the acid from the product by treatment with a mineral acid. The acid melts at 148 to 150° C., and dissolves easily in hot water, alcohol, and ether. Both it and its soluble sodium salt have been recommended as antiseptics and anti-rheumatics but no clinical reports have as yet been forthcoming.

Guaiacol biiodide is a compound made by acting upon crystalline sodium guaiacol dissolved in water with an

aqueous solution of iodine and iodide of potassium. A reddish-brown precipitate is formed which, when collected, washed and dried, has an odor reminding of iodine; it melts on the water-bath, is soluble in alcohol and fatty oils, and readily decomposable. Guaiacol biiodide is believed by its discoverer (Vicario) to be suitable for application as a remedy in tuberculosis.

Styracol, or *cinnamyl-guaiacol,* represented by the formula $C_6H_5.CH.CH.CO_2C_6H_4OCH_3$, is the cinnamic acid ester of guaiacol. It is prepared by the interaction of equal molecules of guaiacol and cinnamyl chloride, the mixture being heated for a short time on a water bath, after two hours' standing. The resultant mass is treated with boiling alcohol, the solution filtered and allowed to cool; long needles are deposited, which are purified by re-crystallization. The pure product melts at 140° C. Styracol is said to be a strong antiseptic, useful when administered internally in chronic vesical catarrh, gonorrhœa, and catarrhal affections of the digestive tract. It was also introduced as a substitute for guaiacol in the treat- of phthisis.

Guaiacol-salol, or *salicyl-guaiacol,* $C_6H_4(OH)COOC_6H_4OCH_3$, is guaiacol salicylate, prepared after the manner of the salols by the action of phosphorus oxychloride on a mixture of guaiacol-sodium and salicylate of sodium. Like the other ethereal salts of guaiacol it is a white, insoluble powder, comparatively without odor and smell; it melts at 65° C., and is decomposed by alkalies into its two components. Decomposition into guaiacol and salicylic acid also takes place in the intestines. It is given to phthisical patients to increase appetite and digestion, in 15 grain doses, and also as an intestinal antiseptic; but no reports as to its use have as yet appeared.

Oleo-creosote is a combination of beechwood creosote with oleic acid, prepared by the aid of phosphorus trichloride. It is a straw-colored oily liquid, containing 35 per cent. combined creosote, insoluble in water, nearly odorless and with faint creosote taste. In the organism it is split up into creosote and oleic acid. It is employed in a similar manner to creosote, and is said to be taken in larger doses without repug-

nance. For adults 45 minims to 2½ drachms pro die, and for children 8 to 45 minims. Subcutaneous injection can also be resorted to without inconvenience (Prevost, Genf).

Asboline, prepared from pine-soot and recommended in tuberculosis (Braconnot), is a yellowish oil consisting principally of pyrocatechol and its homologue, homopyrocatechol, the parent substances of guaiacol and creosol respectively (Béhal).

HYDRACETINE.

Synonyms: PYRODINE; ACETYLPHENYLHYDRAZINE.

$C_6H_5HN\text{-}NHCH_3CO$.

A crystalline compound, which may be regarded as hydrazine (*v.* Hydroxylamine), $H_2N\text{-}NH_2$, in which hydrogen atoms are replaced by the monivalent groups phenyl and acetyl, or as acetanilide in which aniline is replaced by phenylhydrazine.

Preparation.—By heating together phenylhydrazine and acetic anhydride, dissolving the product in boiling water and crystallizing.

$2\,C_6H_5NH\text{-}NH_2 + (CH_3CO)_2O = 2\,C_6H_5HN\text{-}NHCH_3CO + H_2O$

Phenylhydrazine. Acetic anhydride.

Also by the prolonged action of glacial acetic acid on phenylhydrazine, distilling off excess of acid and crystallizing.

The name "Pyrodine" appeared first in literature under the authority of Dr. Dreschfeld in England at the end of 1888, but a few weeks subsequent to the first paper, the above named author explained that pyrodine was an impure acetylphenylhydrazine.

Physical and Chemical Properties.—Colorless hexagonal lustrous prisms, odorless and practically tasteless; melting point 128° to 129° C. Soluble in 50 parts of water at 15° C. and in 8 to 10 parts of the same solvent at 100° C.

Boiled with concentrated hydrochloric acid it splits up into acetic acid and hydrochloride of phenylhydrazine. Like methacetine and phenacetine it forms a colorless solution with sulphuric acid, which is turned red by nitric acid.

Added to a solution of silver nitrate, lustrous metallic silver is thrown down, and similarly it precipitates gold from auric chloride, flecks of metal appearing on the surface of the liquid.

The absence of acetic acid is shown by the neutrality of solutions. Boiled a few minutes with 30 parts hydrochloric acid it dissolves; if chloride of lime solution be added to the cold liquid diluted with 100 parts of water, a yellow tint is produced (violet indicates acetanilide).

Medicinal Uses.—Like the allied body phenylhydrazine, and like hydrazine itself, this compound is a well-marked blood-poison exerting a solvent action upon the corpuscles so as to be capable of producing anæmia; for this reason care has to be taken in its use, both internally and externally, the effect being cumulative, and manifested in malaise, weakness, and a kind of angina.

The substance was first recommended as an antipyretic (Dreschfeld, Guttmann) internally in doses of ⅙ to 1 grain, not exceeding two grains daily and then not more than three days consecutively. Externally in 10 per cent. ointment it has been employed against psoriasis instead of crysarobin. In both these directions, however, the use of hydracetine seems to have greatly fallen off, and no additions have been made to its literature for a considerable time.

ALLIED COMPOUND.

Antithermin, or *phenylhydrazine-laevulinic acid*, $CH_3C(C_6H_5N_2H)C_2H_4COOH$, is the compound of phenylhydrazine with lævulinic acid, a product of the action of concentrated hydrochloric acid on sugar. It occurs in colorless insoluble crystals of neutral reaction, melting at 108° C, and is converted into an anhydride at 170° C. Without reducing action on Fehling's solution. Recommended as an antipyretic (Nicol), and given in doses of 3 grains, 3 times daily in pulmonary phthisis and morbus Brightii, but like all simple phenylhydrazine derivatives requires caution and is frequently accompanied by unpleasant symptoms, a swimming sensation in the head and outbreaks of perspiration (Drobner).

HYDROXYLAMINE HYDROCHLORIDE.

Synonym: Oxyammonium chloride.

$NH_2OH\,HCl$.

A crystalline salt of a base analogous to ammonia.

Preparation.—By the interaction at 0° C. of sodium hydrogen sulphite in concentrated solution and sodium nitrite. The readily soluble sodium salt is by the addition of potassium chloride converted into the difficulty soluble potassium hydroxylaminedisulphonate. By the action of heat upon solution of the latter it is split up into hydroxylamine sulphate and potassium sulphate, which are separated by fractional crystallization, and from the former the hydrochloride is obtained by decomposition with barium chloride.

The two reactions may be represented as follow:—

$$NaNO_2 + 2\,NaHSO_3 = HO.N(SO_3Na)_2 + NaOH.$$

Sodium hydroxylaminedisulphonate.

$$2\,HO.N(SO_3K)_2 + 4\,H_2O = (NH_2OH)_2H_2SO_4 + 2\,K_2SO_4 + H_2SO_4.$$

Hydroxylamine Sulphate.

Physical and Chemical Properties.—Colorless hygroscopic crystals similar in form to ammonium chloride. Soluble in an equal weight of water, also in glycerin and in 15 parts of alcohol. The solutions redden blue litmus, but do not affect congo-paper provided hydrochloric acid be absent.

Chemically the compound is distinguished by an enormous reducing powder, precipitating metallic gold, silver and mercury from solutions of their salts, and throwing down cuprous oxide from Fehling's solution in the cold. The hydroxylamine itself is oxidized thereby to nitrous or nitric oxide and nitrogen acids.

Iron is detected by potassium ferricyanide or thiocyanide; barium by sulphuric acid; and fixed impurities generally by ignition, when no residue should be left. It is distinguished from sal ammoniac by forming a clear solution with 20 parts of absolute alcohol.

Hydrochloric acid is volumetrically estimated by normal potash, using phenolphtalein as an indicator, and hydroxylamine, by excess of decinormal iodine solution, decomposing

the excess with sodium thiosulphate and titrating back with $\frac{n}{10}$ iodine, using starch as an indicator.

$$2\,NH_2OH\,HCl + 4\,I = N_2O + 2\,HCl + 4\,HI + H_2O.$$

Hydroxylamine hydrochloride must be kept in well closed bottles.

The free base hydroxylamine has been prepared in crystalline condition by Bruyn and by Crismer by systematic rectification of the methyl alcohol solution under reduced pressure, and by distillation of the zinc chloride double salt, $ZnCl_2.2\,NH_2OH$, with aniline. Large colorless crystals, melting at 33° C., very hygroscopic and dissolving readily in water.

Medicinal Uses.—Hydroxylamine hydrochloride was suggested as a non-staining substitute for the reducing bodies pyrogallol, chrysarobin and anthrarobin in the treatment of skin diseases. It proved effective in lupus (Eichhoff, Fabry), in mycosis tonsurans, sycosis parasitaria, psoriasis, etc. (Burz). Some authors pronounced it to be dangerous if absorbed (Groddeck), and, like the amine compound below, it is a powerful poison to the blood and generally antagonistic to vegetable and animal life.

DERIVATIVES AND ALLIED COMPOUNDS.

Hydrazine, or *Diamine*, N_2H_4, is a somewhat allied and similarly reducing body. It is also a general poison to animal and vegetable life; germinating cotyledonous plants and algæ, infusoria, crustaceans, and insect larvae, young snakes and rabbits being alike killed by it (Loew and Buchner). Peptone solutions containing 1 per mille of diamine sulphate are no longer able to support bacterial life, and the solutions remain unchanged for weeks. Diamine also kills the germs of mould.

Phenylhydrazine, $C_6H_5NH.NH_2$, the simplest aromatic derivative of hydrazine, is a white crystalline body, melting at about 35° C., and rapidly discoloring on exposure. It is the basis of a number of the newer remedies. In simple combinations, corresponding to those of aniline ($C_6H_5NH_2$) in acetanilide, its physiological action appears too violent, but in more complex combinations, as in agathin and in anti-

pyrine, it is very much modified. Phenylhydrazine is a strongly caustic base, and even its vapors are apt to produce an extremely painful skin affection resembling urticaria (Du Bois-Reymond).

HYPNONE.

Synonyms : ACETOPHENONE ; METHYLPHENYLKETONE.

$C_6H_5COCH_3$.

A liquid compound long known to the chemist and classified among mixed ketones.

Preparation.—By the dry distillation of calcium acetate and calcium benzoate. The crude product (containing about 6 per cent. of hypnone) is purified (from toluol, diphenyl ketone and cumarin) by repeated fractional distillation, solidified by cold, the adhering liquid removed by bibulous paper and again rectified. The reaction by which methylphenylketone is formed is

$$\left.\begin{matrix}CH_3COO\\CH_3COO\end{matrix}\right\}Ca + \left.\begin{matrix}C_6H_5COO\\C_6H_5COO\end{matrix}\right\}Ca = 2\,CaCO_3 + 2\left\{\begin{matrix}CH_3\\C_6H_5\end{matrix}\right\rangle CO.$$

Calcium acetate. Calcium benzoate. Hypnone.

Physical and Chemical Properties.—When pure, hypnone is a colorless oily liquid at medium temperature, with a peculiar odor and a pungent taste. Specific gravity, 1.032 ; at 14° C. it solidifies, melting again at 20.5° C. (Staedel and Kleinschmidt). Very little soluble in water, but readily miscible with alcohol, ether and fatty oils.

Chemically, hypnone has all the properties of a true ketone, but does not form a crystalline compound with sodium hydrogen sulphite. Free acids must not be present, therefore it should not alter blue litmus paper, and the absence of benzaldehyde and cumarin is required by providing that one drop of hypnone in 3 drachms of $\frac{n}{1000}$ permanganate must not decolorize the latter within two minutes.

Medicinal Uses.—First recommended as a hypnotic in 1885 (Dujardin-Beaumetz), being regarded as superior to chloral hydrate and to paraldehyde. Did not prove very successful in the treatment of mental diseases (Rottenbiller),

while also patients soon became habituated to its effects so that the doses had to be continually increased (Seifert). Hypnone reduces blood pressure and slows the respiration, so that care must be exercised in its administration (Grosset). The dose is 1 to 3 minims.

ICHTHYOL.

Synonym: Ammonium Ichthyol Sulphonate.

$C_{28}H_{36}S_3O_6(NH_4)_2$.

The most important of the salts of ichthyolsulphonic acid, prepared from a bituminous mineral of Tyrol which is rich in fossilized remains of fish and sea animals, whence the name "ichthyol" (*ἰχθύς*, fish).

Preparation.—By dry distillation of the bituminous mineral, there passes over, between 100° C. and 225° C., a crude volatile oil. This is treated at 100° C. with an excess of concentrated sulphuric acid, and the resultant ichthyolsulphonic acid precipitated several times by concentrated brine to obtain it free from excess of mineral acid. The ammonium salt is prepared by neutralization of the free ichthyolsulphonic acid with strong ammonia.

Physical and Chemical Properties.—Ichthyol oil before treatment with sulphuric acid contains a high proportion of sulphur—about 10 per cent. (Baumann and Schotten)—combined in a manner not well understood; it cannot be extracted by boiling with aqueous or alcoholic potash, nor by treatment with sodium amalgam. When warmed with methyl iodide no crystalline compound is formed, such as the sulphides of the fatty series are known to yield.

The process of sulphonation outlined above increases the percentage of sulphur to about 17 per cent. in ichthyolsulphonic acid, but the product still contains a certain proportion of unchanged volatile oil, which gives it a peculiar odor. This oil cannot be removed without bringing about decomposition.

The product of the saturation of the ichthyolsulphonic acid with ammonia is a clear, reddish-brown, viscid liquid, with a bituminous odor and taste. It is miscible with water (the

mixtures being faintly acid); alcohol and ether dissolve it in part; petroleum benzene takes up very little. From aqueous solutions hydrochloric acid throws down a dark resinous mass, soluble in ether and in water (but not in dilute acids or solution of sodium chloride). The action of potash developes the odor of ammonia, and the mixture dried and carbonized forms a mass which gives off sulphuretted hydrogen when treated with hydrochloric acid. Dried in a water-bath, ichthyol loses about 45 per cent. of its weight.

Medicinal Properties and Uses.—The application of ichthyol in medicine, according to the very large experience hitherto obtained, depends chiefly upon four factors: (1) its reducing property, (2) its antiseptic action, (3) its vascular contractile effect, (4) its favorable influence on the animal metabolism. From this combination of properties, ichthyol has proved useful as an antiphlogistic, an alterative, anodyne, resolvent, gastric and renal tonic, and astringent. That the substance has a true kolyseptic power, *i. e.*, exerts a restraining influence upon the development of bacteria, has been proved bacteriologically (Fessler, Klein, Latteux), and confirmed repeatedly by practical experience; its peculiar virtues are largely ascribed to the high proportion of sulphur it contains. The bacteriological action of ichthyol is specially developed against the streptococci of pus and of erysipelas, which it kills in dilute solutions in a brief period, and it is always constant (Abel).

The usefulness of the remedy was first brought under the notice of the medical profession in 1883, it being recommended in skin diseases merely (Unna). Since then, as already indicated, the list of affections in which it has been successfully employed has grown to such a length that by some authors the substance has been looked at askance as a "panacea" or "cure-all." It appears, however, that many, perhaps most, of the diseases for which ichthyol has been recommended are caused by or associated with anomalies of circulation and capillary dilatation on which its vascular contractile property has a specific action (Nussbaum, Schweninger). Internally it retards the disintegration of albumens and favors their formation and accumulation (Zuelzer, Charles).

The physiological effect on metabolic changes has been studied by Helmers, and his experiments prove that ichthyol, whilst it has no effect on the transformation of albumen in the body, or, if any, only favors its assimilation, introduces at least one-third of its sulphur into circulation in the juices of the body, which is finally eliminated by the urine, whilst the sulphur excreted with the fæces has also evidently been in the circulation and again secreted by the intestinal glands.

The literature of ichthyol is of very large dimensions, rendering it impossible to deal with it all. The more recent additions are confirmatory of those previously made, and present a few new features of the remedy. It has a remarkable effect—especially when applied externally and given internally simultaneously—upon exudations, not only in gynæcology (Freund, Reitmann, Schoenauer, Kotschau, Kurz, Albertoletti, Bergesio) but also in such affections as pleurisy (A. Mueller); pain is promptly alleviated—this anodyne action is one of the most valuable properties of ichthyol for gynæcological diseases (Lehmann)—and the exudation is gradually reabsorbed.

Even in very dilute solutions ichthyol arrests the development of the bacilli of erysipelas and pus (Fessler, Klein), and practically it has done excellent service in erysipelas (Rosenberg). The surrounding parts being carefully washed, pure ichthyol, the collodion or ointment, is spread over them and the affected area; fever subsides, and the course of the disease is shortened and its severity moderated.

In ulcers of the leg, painting with pure ichthyol is effective (Hartmann); the painted part is covered with cotton wool, unstarched bandage and the stocking. Renewal is necessary every three or four days. Eczema and a long list of skin diseases are beneficially influenced by the ichthyol treatment (Bulkley, McLean, Cranstoun Charles, Iliinsky, Chatelain, and others), and for chilblains it has been pronounced unfailing—a 30 per cent. ointment relieving irritation at once and completely (Macpherson). Persistent sycosis and folliculitis are treated with the best results with ichthyol (Ehrmann), and also the cutaneous forms of venereal syphilis (Segré). In angina 2 or 3 per cent. ichthyol gargles rapidly

relieves the pain and reduces the swelling of tonsils and gums, without being unpleasant in use (Herz). A 10 per cent. ointment with equal parts of prepared chalk and lard effects a speedy cure in dermatitis bulbosa (Jamieson). For rheumatism ichthyol is indispensable (Iliinsky); a 50 per cent. ointment is applied locally and the remedy itself given internally. Its use in surgery generally should also be mentioned.

Internally the remedy has been given and recommended for various affections of the digestive and intestinal tract (Jawitzky), of the kidneys, in syphilis (Peroni), leprosy, etc. During the influenza epidemics attention was called to the value of inhalations of ichthyol (Lorenz). Many more authorities might be mentioned, but only those reports of recent date have been specially referred to.

The use of ichthyol internally in the treatment of venereal disorders and in gynæcological practice has assumed enormous dimensions, and one therapeutical report after another has appeared since the last edition of this book. Its analgesic as well as its astringent action have placed it amongst the most valuable remedies in gynæcological therapy (Polacco) and its specific action in blennorrhagia has made it invaluable (Colombi, Ullmann). In the acute and chronic gonorrhœa of males its germicidal action on the gonococci and its sedative effect on the inflammatory process has been established by clinical experience, and 3 per cent. solutions are authoritatively employed in the Bavarian army for injections.

Taking into consideration the great antiseptic action of ichthyol as proved by many authors, and the interesting conclusions of Helmers—proving the impregnation of the body juices with ichthyol and its favorable influence on digestive and assimilative processes, it is not all surprising to see that ichthyol appears destined to play an important rôle in the treatment of phthisis. According to a preliminary report by Cohn it has now been successfully employed in over 100 cases extending over two years. The remedy was prescribed in 20 parts water, commencing with 4 drops and increasing to 40 drops of the solution three times a day for adults; children between 5 and 12 years of age were given about

half the dose. The cures, which were completed in about 12 months, were due not so much to the direct action of the remedy, but to the extraordinarily improved nourishment of the system induced by its use. No bad effects were experienced other than slight nausea in some cases at the commencement of the treatment.

Ichthyol is prescribed for external use pure, in ointment form with lanolin (10 to 50 per cent.), as liniment with turpentine or an equal weight of a mixture of lanolin and olive oil (with 30 per cent. of chloroform in rheumatism), as soap, etc. In gynæcology it is much used in combination with glycerin (1 of ichthyol in 10), and against erysipelas as a 10 to 25 per cent. collodium (ichthyol and ether, of each 5 parts, collodium 10 parts) with or without the addition of caster oil. A solution in eight parts of a mixture of absolute alcohol and ether, or of chloroform and spirit of camphor (1:4), is employed in neuralgia. The odor of the remedy in these preparations may be disguised by the addition of cumarin, vanillin, or citronella.

Internally ichthyol is given—dose 5 to 20 minims—in milk, cocoa or beer, or in pills (the sodium salt being prescribed). Suppositories are made up with cacao butter, as also pessaries; for the latter purpose capsules containing the 10 per cent. ichthyol glycerin have been used.

DERIVATIVES AND ALLIED COMPOUNDS.

Other salts of ichthyol sulphonic acid are the ichthyolsulphonates of sodium, lithium, zinc and mercury. They all occur as brownish-black, tar-like masses, but the first is the only one of any importance. Being solid it is employed when it is desired to give ichthyol in pill form.

IODOL.

Synonym: TETRAIODOPYRROL.

C_4I_4NH.

A crystalline compound first prepared in 1885 by Ciamician and Silber from pyrrol, the characteristic base of bone oil.

Preparation.—By the interaction during 24 hours of iodine and pyrrol in alcoholic solutions. The mixture is then diluted with water, when the iodol separates in crystalline yellow flocks,

$$\underset{\text{Pyrrol.}}{C_4H_4NH} + 8\,I = 4\,HI + \underset{\text{Iodol.}}{C_4I_4NH};$$

or the formation of free hydriodic acid may be avoided by using aqueous solutions of pyrrol with soda or potash, and of iodine with potassium or sodium iodide, collecting the precipitate, dissolving in alcohol, decolorizing with animal charcoal and reprecipitating. There are also other methods involving the use of metallic oxides for the same purpose.

Physical and Chemical Properties.—Pure iodol is a pale-yellow, more or less crystalline, bulky powder, free from odor and taste. It is practically insoluble in water, and slightly soluble in diluted alcohol. Strong alcohol takes up a third of its weight, which is precipitated from solution by water but not by glycerin. Ether dissolves its own weight of iodol, and fatty oils about one-fifteenth.

Iodol contains 89 per cent. iodine. When heated gradually iodol is unaffected up to 100° to 120° C., but between 140° and 150° C. it is decomposed with the evolution of violet iodine vapors; if the heat is maintained it finally burns away without residue.

Metals, if present, are detected by sulphuretted hydrogen, and iodides by argentic nitrate.

Medicinal Uses.—Iodol was introduced as an iodoform substitute, having the advantages of being odorless and non-toxic. Has been specially recommended for the treatment of syphilitic ulcers (Mazzoni, Szadek), but also for use in general surgery and inflammatory conditions (Wolff, Schmidt, Markus, Pick). A specially prepared crystalline form has been recommended for application to the mucous membrane as not "balling" like the ordinary powder; insufflation of this crystalline iodol has proved useful in ozæna, and it has also been successfully employed in caries of bone, tuberculous ulcers, diseases of the tonsils, trachea and larynx (Schaffer). Recommended in the treatment of eczema of the ear, either as insufflation or ointment (Chatellier).

Internally—in doses of 8 to 15 grains, two to four times a day, in wafers—iodol has been recommended when the long-continued but not too powerful effects of iodine are indicated (Szadek).

Like iodoform, iodol is used as a dusting powder, in alcoholic or ethereal solution, with ether and collodium (iodol 1, ether 5, collodium 50); a 5 or 10 per cent. ointment is also applied. In gynæcology tampons are employed soaked in a solution of iodol, spirit and glycerin (1:16:34). The same solution, or a 10 to 20 per cent. ethereal solution, has been used for injection into fistulæ and abscess cavities. Iodol is believed to stimulate granulation.

DERIVATIVES AND ALLIED COMPOUNDS.

Caffeine-iodol, $C_8H_{10}N_4O_2.C_4I_4NH$, prepared by the interaction of equal molecular quantities of caffeine and iodine, is a greyish crystalline powder, free from odor and taste, and practically insoluble in any of the ordinary solvents. It contains 74.6 per cent. iodol, and is free from the tendency of the latter to separate iodine on long keeping (Konteschweller), but has not made its way into therapeutical practice, though said to possess higher kolyseptic value than iodoform (Spiegler).

Iodolin is the trivial name given to a double compound of iodine chloride with chinoline chlormethylate.

Diiodoform, or *ethylene periodide*, C_2I_4, prepared by treatment of acetylene iodide, C_2I_2, with excess of iodine, preferably in carbon bisulphide solution (Bocquillon). It corresponds to a combination of two molecules iodoform, with separation of hydriodic acid, thus:

$$2\,CHI_3 = C_2I_4 + 2\,HI.$$

Diiodoform crystallizes in beautiful yellow, prismatic needles, insoluble in water, sparingly soluble in alcohol but more freely soluble in chloroform, carbon bisulphide and toluene. When pure it melts at 192° C.; heated quickly it decomposes into carbon and iodine. It contains 95 5 per cent. iodine, and unlike iodoform is nearly free from odor. It is not easily attacked by chemical reagents, but is slowly decomposed by light. On account of its freedom from odor it

is recommended as a substitute for iodoform (Adrian), with which it is equal in antiseptic properties and dermatological value (Hallopeau).

Iodocasein is another substitute for iodoform recently brought forward. It is a yellowish powder without odor, but at present nothing further is known in regard to it.

LANOLIN.

Synonym: ADEPS LANÆ HYDROSUS.

The purified cholesterin fat of sheep's wool containing not more than 30 per cent. of water.

Preparation.—From crude wool fat by emulsification with hydrate or carbonate of the alkalies, and "separation" (into a kind of cream and whey) in centrifugal machines. From the "separated" cream the cholesterin fats are set free by addition of solution of calcium chloride, and the impure lanolin thus obtained purified by repeated melting and washing, and finally by extraction with acetone, which does not dissolve the contaminating calcium soap.

Physical and Chemical Properties.—A whitish, unctuous substance, free from odor. It does not affect moist litmus. Insoluble in water, only partly soluble in alcohol, but readily so in ether, benzene (benzol) and acetone.

Kneaded with water for some time, lanolin should take up about 100 per cent. of water without slipping smoothly off a spatula; preparations containing soap exhibit this absence of adhesiveness.

With respect to the proportion of water present, the B. P. Add., and U. S. P. require that 100 grains heated on a water bath till of constant weight shall yield not less than 70 grains residue. It is further characteristic of a pure preparation that the supernatant layer of fat obtained when the substance is heated with five times its weight of water in a water bath is a clear pale yellow oil. The browning of the supernatant oil on heating is distinct evidence of the presence of deleterious substances that readily decompose.

This supernatant fat (*Adeps Lanæ*, B. P. Add.) should be separated from the aqueous liquid and especially examined. According to the B. P. Add. [2nd Ed.] it should have a melting point between 37.8° C. and 44.4° C. (the former figure is certainly too low, as under 40° C. there is hardly any evidence of melting in anhydrous lanolin), and 10 grains should dissolve almost completely in 14 fluid drachms of boiling alcohol, the greater part separating in flocks on cooling. (The intention here is presumably to distinguish lanolin from glycerin fat.) Ignited with free access of air it must also leave but a trace of ash (0.1 per cent. of inorganic salts); and 50 grains dissolved in 4 fluid drachms of ether, with 2 drops of phenolphtaleïn tincture should not require more than 2 grain measures of volumetric soda solution to produce a permanent red coloration. This test only restricts the allowable amount of free fatty acids present to about 2 per cent. whereas a pure cholesterin fat answers to tests ten times or more stringent. In fact, as a means for guarding the preparation against rancidity from the presence of fatty acids, the looseness of the test makes it valueless, and the amount of alkali required to produce a red coloration should be stated at one-tenth of the amount at least. "Heated with solution of soda no ammoniacal odor should be evolved," so that ammonia compounds must not be present.

Lanolin is also free from chlorine in any form. Boiling with water and testing the separated water with silver nitrate solution will detect the presence of free hydrochloric acid or of chlorides, but organic chlorine compounds, which are the most dangerous impurities, are overlooked. The addition of an alcoholic solution of silver nitrate to a boiling alcohol solution of the fat is not to be recommended, as a turbidity produced by depositing fatty matter may be set down as chloride. The Carius method is most reliable. 0.5 gm. lanolin heated with 10 cc. nitric acid (free from chlorine) and 0.1 gm. silver nitrate in a sealed tube at 170° to 180° C. for 5 hours is completely oxidized, and the clear blue solution should be free from any deposit of silver chloride. Fusion with potassium nitrate and lime and examination of the residue should give the same result.

Of the identity tests for cholesterin that of Salkowsky is adopted, involving the production of a purple red color when a chloroformic solution is gently poured over sulphuric acid. If the operation be carefully performed the surfaces of contact show a fiery brownish-red zone, which recalls the color of bromine, while the supernatant layer of chloroform immediately above has a violet tint and the upper portions remain colorless.

Liebermann's test, which involves the production of a color not given by glycerin fats, consists in dissolving about two grains of lanolin in about 1 fluid drachm of acetic anhydride, and dropping concentrated sulphuric acid into the solution; a rose-red color is produced, which rapidly changes to green or blue (Cholestol reaction).

Another character which distinguishes lanolin from glycerin fats is that it cannot be saponified to any extent by the action of aqueous alkalies. The saponification of lanolin —*i. e.*, the separation of the fatty acids from the cholesterin —is only effected by heating the substance with alcoholic potash or by melting with the solid hydrate. The peculiar stability of lanolin (its non-liability to rancidity) must be ascribed to this firm combination between the cholesterin and the fat acids.

The fatty compounds of lanolin are ethereal salts of cholesterin ($C_{27}H_{46}O$) and isocholesterin ($C_{26}H_{44}O$) principally with cerotic and palmitic acids, and also with small quantities of stearic, oleic, capronic, isovalerianic and normal butyric acids (De Sanctis).

A saponification test for the presence of glycerin fats or of vaseline or other hydrocarbons in cholesterin fats by Helbing and Passmore, is based upon the absolute indifference of hydrocarbons to alcoholic potash and the lower combination equivalent of cholesterin fats with alkalies as compared with glycerin fats. 5 grams fat are heated in a stout securely fastened bottle at 100° C. for two hours with 20 cc. of 10 per cent. alcoholic potash, the contents then diluted to a litre and the uncombined alkali titrated with standard acid and phenol-phthalein. Petroleum bases being unsaponifiable and insoluble in the alcoholic solution can be separated and

determined direct. A thoroughly purified wool-fat combines with about 8½ per cent. of caustic potash (KHO), whilst glycerin fats give much higher figures (Lard 20 per cent.; olive oil 18 per cent.; cocoa-nut fat 25 per cent.), and mixtures in proportion.

Medicinal Uses.—The fat peculiar to wool and keratin tissues generally was used in medicine centuries ago, but in a very impure condition, under the name "oesypus." This malodorous and irritating substance fell out of use and was altogether forgotten until the introduction of the purified cholesterin-fat by Prof. Liebreich, who made an intimate study of the properties of lanolin. Three factors have been of great weight in determining the permanent retention of the substance in materia medica, as an application to the skin and as a vehicle for the external employment of medicaments of all kinds; these are (1) its great stability, *i. e.*, its resistance to the agents that induce rancidity; (2) its property of taking up a large quantity of water without losing its ointment-like consistence, and (3) the readiness and completeness with which it is absorbed by the skin. To these must be added, as no less important, that lanolin is perfectly free from any irritating constituents.

When lanolin is rubbed upon the skin it is rapidly taken up by the membrane—to which in a sense it naturally appertains—any medicaments mixed with it being at the same time absorbed (Liebreich, W. G. Smith, Paulowsky, Vogel, Bernatzek, Wende, Shoemaker, and others). Its use is therefore indicated in all cases where it is desired to saturate the skin with fat, as for instance in a certain class of skin diseases, or to affect the deeper tissues as in the inunction treatment of syphilis. Experiments on the length of time after which medicaments (*e. g.*, iodine preparations) applied with lanolin to the skin can be detected in the urine, have established the unequalled rapidity with which the substance is absorbed. At the same time this energetic absorption makes perfect purity the more essential. The irritating foreign ingredients (*e. g.*, fatty acids of an impure preparation, cholerine decomposition products) would be applied

under circumstances the most favorable to the production of a maximum irritant effect.

In consequence of the readiness with which lanolin absorbs water and aqueous liquids, it adheres well to the mucous membrane—a great advantage, of course, in the medication of that tissue. It reduces irritation, and is employed in gonorrhœa as ointment, bougies, or injection, and for healing erosions and allaying irritation of the intestines.

Searching experiment has proved that lanolin resists the decomposing action of micro-organisms; it contains nothing which these forms of life can split up and feed upon, and hence a thin layer is a perfect barrier to their progress, while, further, the base itself is always free from germs (Fraenkel, Gottstein).

The advantages of lanolin over other ointment bases are so marked that it has been almost exclusively and universally adopted for the application of the newer remedies in ointment form. Even acids, acetate of aluminium, chloride of calcium, hydrogen peroxide, sulphurous acid, and other substances of which hitherto ointments could not be usefully prepared, may be successfully applied with lanolin (Unna). The sole practical objection to the use of lanolin for ointments containing only solid ingredients is its stickiness, and this is readily overcome by mixing it, as the writer has previously recommended, with liquid paraffin and ceresin, or with one-third of its weight of vaselin (*i.e.*, petrolatum). This diluted lanolin—or unguentum lanolini, as it was named by the deviser—meets all the requirements of a good ointment base, and its value has been confirmed by the experience of numerous medical authorities. It is the most suitable form in which lanolin can be prescribed (Paschkis).

Unguentum lanolini with 60 per cent. of water has been warmly recommended as an extraordinarily active remedy for the relief of itching. The evaporation of the suspended water cools the epidermal surface and reduces capillary hyperæmia; the ointment is especially valuable in the treatment of measles, scarlet fever, chicken-pox, etc. (Klein). The preparation has not the sometimes unpleasant adhesiveness of the unmixed lanolin, while it has all the useful

therapeutical properties of the latter. Any application in solid or liquid form can be readily mixed with it, and the ointment so made will keep good and free from rancidity for an indefinite length of time. The writer has samples of mercurial ointments made with lanolin ointment which have kept unchanged for two years.

The resistance of lanolin to chemical agents which tend to decompose most organic substances lead to its use for the purely pharmaceutical purpose of massing permanganate of potassium and some other refractory substances for pills.

As a cosmetic, lanolin plays an important part, each of its distinctive properties being of special significance in this application. In fact toilet lanolin preparations entirely take the place of the old-fashioned ordinary cold cream and of vaseline preparations and cosmetics, lanolin being the natural fat of the skin and keeping it always in a proper condition. Particularly against sunburn and freckles lanolin seems to be the only ointment which acts as a protective. Cold creams, pomades, milks, emulsions, soaps, etc., are made with it, of which some of the many formulæ may be given as examples. Toilet lanolin is unguentum lanolini (*vide supra*), perfumed with vanillin, lilac and otto of rose. Lanolin-pomade can be prepared from 85 parts of the anhydrous basis and 25 parts of coco-nut oil; lanolin-milk is an emulsion of 10 parts of lanolin, 1 part of borax and 100 parts of rose water. For injection into the urethra a mixture is made of anhydrous lanolin 25 parts, almond oil 75 parts, with the addition of zinc sulphate ½ part (dissolved in 4½ parts of water) or of salicylic acid ¼ part, or of resorcin 1½ parts. Lanolin (anhyd.) and soft soap, in the proportions of 4:5 respectively, form sapolanolin, by means of which mercurials and other remedies are applied to the skin. Another preparation used as a basis in dermatology is anhydrous lanolin 4 parts, wax 4 parts and olive oil 2 parts; 1 part of lanolin (anhyd.) with 2 of benzoated lard and 3 or 6 of water form excellent bases for cooling ointments or creams (Unna). In the manufacture of the so-called "superfatted soaps" a good many manufacturers now use lanolin as the most suitable form of adding the excess of fat. From 5 to 10 per cent. of lanolin

is added to the soap mass with or without the addition of a small proportion of olive oil.

Various other preparations of wool-fat have been introduced as imitations of lanolin. *Adeps lanae*, or *Lanain* is a cholesterin fat, which, although having a lower melting point, possesses the stickiness of anhydrous wool-fat. It further contains chlorine decomposition products, detected as chloride by the Carius test (*vide supra*), and also by the browning of the fat on heating, which renders its employment as an ointment base ill-advised (Liebreich, Rothmann). *Agnine*, an American product of more solid consistency, said to be prepared by the distillation of wool-fat, contains between 30 and 40 per cent. free fatty acids. *Anaspaline* is an impure wool-fat mixed with about 25 per cent. vaseline, but is no longer in the market.

DERIVATIVES AND ALLIED COMPOUNDS.

Thilanin, or brown, sulphurated lanolin, is a preparation prepared by the action of sulphur upon lanolin; the product, which contains 3 per cent. of the active ingredient, is an ointment-like mass with about the same consistence as lanolin, dark yellowish-brown in color, and with the characteristic odor of sulphurated organic compounds. The original object aimed at in preparing it was to obtain a body possessing all the useful properties of a remedy of the good old times—oleum lini sulphuratum—without its disadvantages.

The preparation has been used in a number of cases of eczema of all degrees of intensity and extent, in the most different parts of the body. In some of them the usual remedies had been tried in vain. The application of thilanin was followed by alleviation of irritation and itching, and subsequent restoration of the skin to its normal condition and functions. In eczema of the scalp, where cutting the hair very short is not feasible, the ointment must be diluted with oil or aqueous liquids—which it absorbs as well as lanolin—in order to enable it to be brought into intimate contact with the affected parts.

A beneficial influence was also observed upon sycosis, herpes, acne, psoriasis, and other forms of skin disease

(Saalfeld). Experience showed that it had a more energetic effect than the usual indifferent remedies (Ung. Hebræ, borovaselin, or borolanolin) while at the same time perfectly non-irritating; on the other hand, it relieves the itching of a number of skin affections. In a later publication Saalfeld produces further evidence as to the advantages of employing thilanin, especially in dermatitis and icthyosis.

The following fatty mixtures have also been recommended as new ointment bases, but have met with very little application, none of them possessing the advantages of lanolin.

Mollin is a neutral soap with 17 per cent. of added fat, introduced several years ago, but which has fallen into disuse.

Resorbin, an emulsion of almond oil and some wax with water by the addition of gelatine or soap, has like lanolin a cooling effect on the skin owing to gradual evaporation of water, but its use as an ointment base is restricted, as ointments prepared with it do not keep.

Vasogene, a thick yellowish-brown liquid of slight alkaline reaction and peculiar odor, forming a permanent white emulsion with water, is said to be the product of a peculiar oxidation process obtained from vaseline.

Vaselon is a solution in vaseline oil of the products of the dry distillation of stearic acid or of beef tallow with lime, termed styrone or margarone.

Serum paste (*Pasta serosa*) and *serum powder* are the names under which Kohlmeyer puts forward a mixture of sterilized ox-blood serum with zinc oxide. The serum preparations are mixed with remedial agents and are supposed to practically substitute the natural process of granulation, and on the other hand promote absorption by the skin. No clinical report has appeared, and so far the considerations appear to be only theoretical.

METHACETINE.

Synonyms: PARA-ACETANISIDINE. PARA-OXYMETHYLACETANILIDE.

$C_6H_4.OCH_3.NHCH_3CO.$

A crystalline compound differing from acetanilide in the substitution of a hydrogen atom in the benzene nucleus by the oxymethyl group—OCH_3.

Preparation.—Nitro-phenol is first prepared by the action of melted phenol upon nitric acid (specific gravity 1.34), separation, washing and steam distillation of the oily liquid formed. Orthonitrophenol passes over, and pure paranitrophenol is obtained from the residue by recrystallization from hot concentrated hydrochloric acid. By the action of soda lye, sodium paranitrophenol is formed, and this, by heating with methyl chloride, yields nitranisol. The reduction of nitranisol to anisidine, and the action of glacial acetic acid upon the latter complete the process, the compound being purified by repeated crystallization from boiling water. The principal reactions may be represented as under:—

$$\underset{\text{Phenol.}}{C_6H_5HO} + HNO_3 = H_2O + \underset{\text{o- and p-Nitrophenol.}}{C_6H_4OHNO_2}$$

$$\underset{\text{Sodium p-nitrophenol.}}{C_6H_4ONaNO_2} + CH_3Cl = NaCl + \underset{\text{Nitranisol.}}{C_6H_4OCH_3NO_2}$$

$$C_6H_4OCH_3NO_2 + 6\ H = 2\ H_2O + \underset{\text{Anisidine.}}{C_6H_4OCH_3NH_2}$$

$$C_6H_4OCH_3NH_2 + CH_3COOH = H_2O + \underset{\text{p-Acetanisidine.}}{C_6H_4OCH_3NHCH_3CO}$$

Physical and Chemical Properties.—Lustrous scaly crystals, free from color (or feebly reddish); odorless and melting at 127° C.; at higher temperature distills unchanged. Scarcely soluble in water at 15° C. (1:530); readily so in the same solvent at 100° C. (1:12); the solutions should be neutral. Also abundantly taken up by alcohol, acetone, chloroform, glycerin, and fatty oils, especially if warmed; less so by benzene, and only very slightly by carbon bisulphide, petroleum benzin, ether and essential oils.

The absence of sulphates, chlorides and iodides is ensured by the usual tests, and inorganic impurities generally by ignition on platinum foil. The compound should form a colorless solution with concentrated sulphuric or hydrochloric acid (carbohydrates darken). With concentrated nitric acid it gives an immediate orange color, and on cooling a crystalline yellow nitro-product separates. The distinction of methacetine from acetanilide, phenacetine, and exalgine is detailed under the properties of the last-named body, and in the monograph on acetanilide.

Like acetanilide (*q. v.*) methacetine gives the indophenol reaction. When boiled with an insufficiency of water to form a solution methacetine forms an oily liquid, which on cooling solidifies. Phenacetine similarly treated does not melt.

Medicinal Uses.—This compound was first recommended in 1888 as an antipyretic for children and enfeebled persons (Mahnert), having the advantage of exerting no solvent effect upon the red blood corpuscles; it is well-borne, and no malaise, tinnitus, cardiac weakness or exanthem follow its adminstration (Seidler, Mosler, Heinz, and others). The only unpleasant effects are the sometimes violent outbreaks of perspiration, ½ to 1 hour after the dose (Mahnert, Seidler), and a few cases of collapse after comparatively small doses are recorded (Mahnert, Heinz, Seidler). Methacetine has done good service as an antipyretic and analgesic, producing very favorable results also in acute rheumatism. Given in doses of 5 to 6 grains two or three times daily. In cases of ileo-typhus, tuberculosis, etc., with moderate fever, reduction to the normal was effected by comparatively small doses, but where the fever was more intense, larger quantities had to be given. The effect appears very soon after the dose (at the most in half an hour), and the fall of temperature lasts for about an hour, rising then again gradually, sometimes with rigors (Mahnert, Seidler, Kapper). According to some observers, the reduced temperature can be maintained by the administration of divided doses of 3 grains (Masius).

METHYLAL.

Synonym: Methylendimethylether.

$CH_2(OCH_3)_2$.

One of a group of bodies termed "acetals." This member was first prepared pure in 1839 by Malaguti.

Preparation.—By the interaction of methyl alcohol, manganese dioxide and sulphuric acid, distillation of the product and purification by repeated fractional distillation

and removal of water by potash. The reactions consist first in the oxidation of the methyl alcohol to formaldehyde and the reaction of this with undecomposed methyl alcohol, thus:

$$CH_2O + 2\,CH_3OH = H_2O + CH_2(OCH_3)_2.$$

Physical Properties.—A limpid, colorless liquid, with a penetrating ethereal odor, of specific gravity 0.855 and boiling point 42° C. Soluble in water (1:13), in alcohol, ether and in fatty and ethereal oils. Like chloroform it is not easily inflamed. It is not altered by alkalies, but is decomposed by concentrated sulphuric acid. The solutions must be neutral. Aldehyde and methyl alcohol are detected, if present, by the decoloration effected when one drop of volumetric potassium permanganate solution is added to a solution of five drops in three drachms of water, with 10 drops of dilute sulphuric acid.

Medicinal Uses.—Methylal was first recommended as a hypnotic in 1886 (Personali). The first effect was described as a transient period of excitement, on which followed deep and quiet sleep. The respiration was somewhat slowed, the pulse increased in frequency, blood pressure and temperature somewhat reduced, and reflexes weakened. The remedy was principally excreted through the lungs, and hence its effects were only of short duration. Methylal has been employed in mental diseases; in the delirium of alcoholism and in the beginning of simple psychoses with nocturnal excitement it was ineffective (Mairet, Combemale, Lemoine), but proved effective in the later stages of the diseases, in the insomnia of dementia and in progressive paralysis. Subcutaneously, in doses of 1½ minims, diluted with nine parts of water, methylal has been successfully given in delirium tremens; so far as present experience goes it is the best sedative and hypnotic in delirium tremens (v. Krafft-Ebing).

Methylal has been used as an anæsthetic, and externally in the form of ointments and liniments against pain; the literature relating to these applications is meagre. It would appear to be effective as an antidote to small quantities of

strychnine (Motrokin, Personali), but worse than useless if a fatal dose has been taken (Langgaard).

The average dose as a hypnotic was given as 1¼ drachms, in aqueous solution with syrup or in some viscid vehicle. For some years however little or nothing has been heard of methylal, and it seems to have been almost entirely displaced by later remedies, although it is said to be still prescribed in France with good results.

ALLIED COMPOUND.

Formethylal is a crude methylal, containing also formic acid and methyl alcohol.

METHYL CHLORIDE.

Synonyms: CHLORMETHYL; MONOCHLORMETHANE.

CH_3Cl.

A gaseous compound first prepared by Berthelot.

Preparation.—By the interaction of molecular proportions of methyl alcohol and hydrochloric acid, with or without the addition of chloride of zinc. The gas produced is washed by leading it through water, sulphuric acid, soda solution, then sulphuric acid again, and finally compressing it in metallic cylinders under a pressure of 3 to 7 atmospheres.

Physical and Chemical Properties.—A colorless gas with an ethereal odor; it burns with a greenish flame though it is not highly inflammable. Soluble in one-fourth its volume of water, much more so in ethyl or methyl alcohol, and freely in ether and chloroform. Under a pressure of five atmospheres at normal temperature, or under normal pressure at —25° C., it is a liquid with a specific gravity of 0.9915 (at —23.7° C.), and boiling point of —21° C. This liquid should be neutral to test paper and unaffected by silver nitrate or potassium iodide and starch paste.

Medicinal Uses.—The compressed liquid form of methyl chloride was recommended for use as spray against

neuralgia, pruritus, and spinal pains after railway accidents (Debove, Steiner). One writer raised a warning voice to the effect that unless care were taken in its application phlegmones, gangrene, erysipelas and severe pigmentation might occur (Schuchardt), but no other evidence of this kind has been published. Any evil effects from excessive employment can be avoided by ordinary care, and its success in sciatica, lumbago and intercostal neuralgia is very marked (Hertmanni).

As compressed methyl chloride absorbs a large quantity of heat in reassuming the gaseous condition it has been used to produce local anæsthesia. A stream of the liquid is directed upon a tampon of wool and silk placed over the surface to be anæsthetized; the liquified gas at first saturates the tampon, and then rapidly evaporating therefrom absorbs the heat from the adjacent parts of the body and leaves them bloodless and insensitive. It has been employed thus against local pain, and in minor surgery. When sprayed directly upon the area it is desired to anæsthetise the stream should not be maintained more than two or three seconds at a time, though the application may be repeated at intervals according to the necessities of the case. Under its use in this way minor operations have been very satisfactorily performed, and absolutely without pain (Berezovsky). Over the ether spray it has the advantages of more rapid effects, non-inflammability, and freedom from irritant effects upon the mucous membrane.

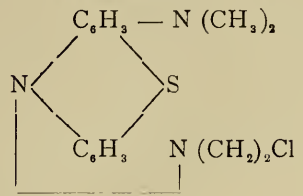
DERIVATIVES AND ALLIED COMPOUNDS.

Richardson's compound-liquid is a mixture of ether and chloroform saturated with methyl chloride. It was recommended as a substitute for pure chloroform as an anæsthetic, but does not appear to have any advantages over the latter.

Coryl, or *Chloryl*, is the name given to a mixture of methyl chloride and ethyl chloride (see under **Ethyl bromide**), which is liquid at 0° C. The anæsthesia is not so strong as that produced by ethyl chloride alone.

METHYLENE BLUE.

Synonym: Tetramethylthionine Chloride.



A sulphuretted diphenylamine compound, also classed as an "aniline color."

Preparation.—By oxidation of dimethylparaphenylenediamine by ferric chloride in the presence of the necessary quantity of sulphuretted hydrogen, or by the interaction of the hydrogen sulphide and nitrosodimethylaniline and oxidation of the product in strong sulphuric acid solution. The patented process consists in oxidation of *p*-amidodimethylaniline in the presence of sodium thiosulphate when *p*-amidodimethylaniline thiosulphonate is formed. From this methylene blue can be obtained in two ways, (*a*) by mixing with dimethylaniline, treating with chromates and boiling the resultant tetramethylindamine thiosulphonate with zinc chloride solution, or (*b*) by reduction to *p*-amidodimethylaniline mercaptan and oxidation of this with chromates in the presence of dimethylaniline. Leucomethylene blue (the dihydro additive produce of the base) is actually formed in both these processes, and is easily converted into methylene blue by oxidation.

Physical and Chemical Properties.—The methylene blue (ethylene blue O) of commerce is a hydrochloride or a zinc chloride double salt of the coloring base. The preparation which has been used in medicine was described as free from zinc, being a hydrochloride of the pure base tetramethylthionine. Small indigo colored scaly crystals with a bronze-like tinge, and dark green in transverse fracture. Slightly soluble in water—up to 3 per cent. (Brunner)—forming a deep blue solution, which is changed by sulphuric acid to bright green, and from which strong potash solution throws down

a dark violet precipitate. In the presence of alcohol, water takes up more. The solution gives no precipitate with sulphuretted hydrogen (absence of zinc, arsenic and lead).

Medicinal Uses.—Methylene blue was first applied medicinally in 1890 as an analgesic in neuralgic and rheumatic affections; its use in this way was suggested by its special affinity for the nervous system, particularly for the axial cylinders of the sensible and sensory nerves (Ehrlich and Leppmann). The remedy was given either subcutaneously in doses of ⅓ to 1 grain, or internally in gelatin capsules in doses of 1½ to 8 grains. Good results were obtained in angeiospastic migraine, in simple neuralgia and acute rheumatism (above named authors, Combemale and François), as also in the pleuritic pains of tuberculous patients (Althen). Pains disappeared two hours after doses of 3 grains, and returned only after six to eight hours. No unpleasant effects of any kind were observed save vomiting in one case (cardiac disease with acute gastric catarrh).

As methylene blue has proved the best stain for the plasmodia found in the blood corpuscles of malarial patients it was also tried against intermittent fever, with pronounced success in 1½-grain doses five times daily. The febrile attacks disappear in the course of the first few days, and the plasmodia from the blood after a week at the most (Guttmann and Ehrlich). A solution of 1 in 20000 immediately checks the movements of the plasmodia in the blood, and kills the parasites in half-an-hour; the dye circulates in the blood as leucomethylene blue owing to the reducing action of the alkaline blood, and the colorless base has a stronger microbicidal action than the dye on account of the avidity with which it takes up oxygen (Rosin). Excellent results have been obtained in therapeutical practice by several authors (Parenski and Blatteis, Neumann, Fratnich), who found that it was effective in cases where quinine failed or was productive of unpleasant symptoms. Methylene blue appears, however, to be subject to variations in composition, as several observers have noticed disturbances with some makes, probably arising from metallic impurities—vomiting and diarrhœa were observed in four out of five cases by Ketli—and

it therefore appears necessary to obtain the remedy from a good source.

The administration must be continued—dose 8 grains *pro die*—eight to ten days after the disappearance of the fever, and in very severe cases even longer. Here also no serious by-effects were observed; slight vesical irritation or catarrh of the digestive tract sometimes appeared but this was easily combated by the administration of powdered nutmeg, of calcined magnesia, or of linseed tea.

Methylene blue has also been employed with advantage in various cancerous affections. Anascara and pains disappear in carcinoma uteri and tumors decrease in size by administration of 3 grains in capsules daily for three weeks (Rudish and Einhorn). The locality of cancerous surfaces is reduced and defined in carcinoma mammæ by injections of 0.5 per cent. solution, hæmorrhage and pain at the same time disappearing (Ambrosio), and Lindner also employed it for the removal of a malign tumor on the left cheek. In five cases of epithelioma painting daily with a 10 per cent. alcoholic glycerin solution of the remedy, after previous cautery with 0.2 per cent. chromic acid, effected a complete and rapid cure, leaving only slight scars (Darrier).

Externally, in aqueous solution for irrigating empyema cavities, in 10 per cent. admixture with cacao-butter (as pencils or suppositories), or internally in substance (capsules or wafers), methylene blue has been given with satisfactory results in various tuberculous conditions. In pulmonary phthisis a dose of 1½ grains was given the first day, increased on the second to 3 grains, on the third to 4½ grains, and so on until 24 grains were taken in the 24 hours. Expectoration diminished and general well-being improved; the results, compared with those obtained from the creosote treatment, encourage more extended trials (Althen). In pharyngeal tuberculosis the powdered substance was also applied to the affected areas (after cocainisation); in scrofulous swelling of the glands of the neck it was injected in 17 per mille solution. In all cases healing was effected. Most satisfactory results were obtained in endometritis and other diseases of women by combined local (pessaries) and gen-

eral treatment; a daily dose of 8 grains was never exceeded here.

DERIVATIVES AND ALLIED COMPOUNDS.

Pyoctanin.—Under this name two dye-substances were introduced into medicine during the second half of 1890, on the recommendation of Professor J. Stilling, who carried out (in association with Dr. J. Wortmann) a series of researches on the antibacterial properties of the aniline dyes. The so-called "blue-pyoctanin" is apparently one or other (or mixtures of two or more) of certain compounds classed as *methyl-violets*, while "yellow-pyoctanin" is one of the group of dyes known as *auramines*. Methyl-violet, or pyoctanin coerulum, is penta- and hexa-methylpararosaniline, and auramine, the mixed hydrochlorides of pyoctanin aureum, is an imido-compound of tetramethyldiamidobenzophenone, represented by the formula, $2\,[(CH_3)_2.N.C_6H_4]C{:}NH$. Solutions of the blue compound (½ to 4 : 10,000) were recommended in general surgery, and of the yellow for ophthalmic practice. Dusting powders, ointments, and dressings were also introduced into commerce. Early in the history of these compounds there appeared a number of reports, of which some recorded the non-success of the antiseptics, and others warned against irritation and eczema which might be caused around the points of application (Braunschweig, Mautner, Roeloff, Patrzek). On the other hand favorable results were obtained in nasal diseases (Bresgen, Schemmann, Cholewa), in croup, by inhalation of a 5 per mille solution (Kellerer), in eye diseases, ulcus molle and gummata (Petersen, Wanscher), and in the treatment of tumors (v. Mosetig-Moorhof). Sometimes a cure and in other cases improvement followed the use of pyoctanin in certain malignant tumors (v. Sehlen, Einhorn, Bachmaier, Boas), and its use in this direction has increased during the last two years.

It seems that the substances introduced as pyoctanin are of variable composition (Liebreich), and it is, therefore, preferable to use a single definite compound from the same group (methyl violet) specially prepared for medicinal use.

Excellent results have been reported of the use of pyoctanin coerulum in diphtheria, for which fresh warm saturated

solutions have been employed in painting the membranes (Jänicke, Taube, Höring).

Apyonin (from α privative and πυον pus) was put forward as a rival to pyoctanin in ophthalmic practice. It was decribed as a yellow crystalline powder, little soluble in water, hot or cold, still less so in ether, but abundantly in alcohol. When carefully heated it sublimed, and at higher temperatures burned away without residue. The concentrated aqueous solution was neutral; its color was altered by neither hydrochloric acid nor nascent oxygen. Potash produced a white precipitate, soluble in alcohol. It has been affirmed to be identical with yellow pyoctanin, but did not succeed in attracting any attention.

Benzo-phenoneid.—According to the discoverers (Galezowski and Petit) this is a definite compound produced by the decomposition of an aniline dye. It is said to be equal as a germicide to pyoctanin, soluble in 100 parts of water, and neither caustic nor irritant. Good results have been obtained in the treatment of corneal ulcers, purulent keratitis, and other ophthalmic affections, but it does not appear to have gained a permanent position amongst the remedial dyes.

Antirheumatin is a compouud of sodium salicylate and methylene blue introduced by Kamm. It occurs in dark-blue prismatic crystals, soluble in water and alcohol, and has the taste of salicylic acid. Recommended as an antirheumatic in doses of 1 to 1½ grains in pill form every two or three hours.

METHYLENE CHLORIDE.

Synonym : Dichlormethane.

CH_2Cl_2.

Preparation.—By the action of chlorine on marsh gas, on monochlormethane or on diiodmethane. Also more practically by the reduction of chloroform (in alcoholic solution) by zinc and hydrochloric acid, the product being mixed with water, the specifically heavier liquid separated and purified

by successive treatment with soda solution, sulphuric acid, water, chloride of calcium and fractional distillation.

Physical and Chemical Properties.—A colorless liquid, resembling chloroform in odor and solubility; specific gravity, 1.36 at 15° C.; boiling point, 41.6° C. Not readily inflammable, though the vapors burn with a green-edged flame. When pure, methylene chloride is decomposed by light, similarly to chloroform, and the addition of a small proportion of absolute alcohol is therefore recommended.

Chloroform, if present, raises the specific gravity. Ethyl or methyl alcohol added as well as chloroform to prevent detection by the gravity are separated by shaking with water, and the dried and redistilled methylene chloride examined again. The separated washing water should give no turbidity with silver nitrate (chlorinated decomposition products) nor blue color with zinc iodide and starch (chlorine); it should also be neutral to test paper (hydrochloric acid).

Medicinal Uses.—This compound was recommended as a substitute for chloroform, being expected to be less dangerous than the latter owing to its less chlorinated constitution (Eichholz and Geuther). It was particularly used and recommended in gynæcology, but other physiologists (Nussbaum, Breisky and Kapeller) record the production of clonic spasms, nervous disturbances, and even death after its use.

Methylene chloride has also been used in the form of spray as a local anæsthetic.

DERIVATIVES AND ALLIED COMPOUNDS.

English methylene chloride, or *méthylène*, is a mixture of ethyl ether and methylene chloride; it must be carefully distinguished from the definite chemical compound described above. Was recommended as a safe anæsthetic in quantities of about 1 to 2 drachms for minor, or 2 to 6 drachms for larger operations (Richardson), but is not so free from danger as its originator believed; deaths after its use have been recorded (Lawson-Tait).

A mixture of chloroform and methyl chloride has also figured in commerce as "methylene chloride."

NAPHTALENE.

Synonym: NAPHTHALIN.

$C_{10}H_8$.

The typical and simplest member of the so-called naphtalene series of hydrocarbons, with the general formula C_nH_{2n-12}.

Preparation.—Abundantly present in the fraction which comes over between 180°—220° C. in the distillation of coal tar; it separates from this fraction on cooling as a brown mass, and is purified by the action of soda and sulphuric acid, followed by repeated sublimation. Synthetically obtained by the action of heat on phenylbutylene—a product of the action of sodium on a mixture of benzyl chloride and allyl iodide.

Physical and Chemical Properties.—Large lustrous scales, with a penetrating odor, and a burning aromatic taste; it melts at 80° C., readily sublimes, and boils at 218° C. It readily passes over with the vapor of water. Naphtalene is insoluble in water, difficultly soluble in cold but readily in hot alcohol, in ether, chloroform, fatty and essential oils, and in hydrochloric and acetic acids without forming salts. By oxidation it is readily converted into phtalic acid, $C_6H_4(COOH)_2$, from which benzoic acid and certain important coloring agents, such as phenolphtalein and eosin, are prepared.

Naphtalene should be colorless and without action on moist blue litmus paper; on platinum foil it should burn away without residue. If quite pure it remains colorless, and the physical constants are as given above. Further, it must dissolve in concentrated sulphuric acid when warmed gently without color.

Medicinal Uses.—Naphtalene has been employed in medicine chiefly in virtue of its antiseptic and disinfectant properties. Externally in 10 to 12 per cent. solution in linseed or olive oil against itch (Fürbringer), and in ointment form (5 to 10 per cent.) in the treatment of a series of skin diseases, as eczema chron., psoriasis, lepra vulgaris, etc. Has also found application as dusting powder (with 2½ per cent. of bergamot oil to cover the odor), as spray (ethereal solution), gauze and wool in the treatment of wounds.

Internally largely varied results have been yielded, possibly due in some measure to impurity in some of the specimens; some observers record a dangerous action on the kidneys (Magnus), others that in large doses it destroys the red blood corpuscles (Panas, Dorr, Hess, Kolinski). Excellent results have sometimes followed its use in 5-grain doses against typhus, fever and diarrhœa being reduced and the duration of the disease lessened (Wolff). Naphtalene has also been recommended as a safe and reliable anthelmintic in doses of 15 grains (children 5 to 8 grains), with castor oil and bergamot as a corrective (Mirovitch). Only naphtalene recrystallized from alcohol should be dispensed for internal use. Its general efficacy has been recognized by its introduction into the United States Pharmacopœia. Inhalations have done good service in the treatment of whooping cough; only consumptives are not benefited—(of diagnostic value)—(Chavernec). Recommended further as an expectorant in diseases of the respiratory tract, in pills, powders and lozenges, and for irrigation (Rossbach).

Naphtalene can be made into pills by mixing with half its weight of powdered marshmallow root and massing with mucilage. A coating of flexible collodion is preferable to keratin (Bernbeck).

Being poisonous to lower forms of life naphtalene is employed as a preservative of collections, clothes, etc., against the attacks of insects and the like. A small quantity of camphor or benzoic acid is said to largely cover the odor of the compound—sometimes considered disagreeable—without reducing its value as a preventive of moth, etc. A solution of naphtalene in perfumed paraffin oil is also recommended as a preventive against the stings of insects.

NAPHTOL.

Synonym: Iso-Naphtol, β-Naphtol.

$C_{10}H_7OH$.

A crystalline compound resulting from the substitution of a hydrogen atom in the double ringed naphtalene $C_{10}H_8$ by a hydroxyl group, and bearing the same relation to naphtalene as phenol to benzene.

Preparation.—By the action of fuming sulphuric acid on naphtalene for several hours at 200° C. The β-naphtalene sulphonate which is chiefly produced is dissolved in water, neutralized with chalk, the calcium salt crystallized out (the α-salt is more soluble), dissolved in water, converted into sodium salt, and the latter decomposed by melted soda, as shown under :

$$C_{10}H_7SO_3Na + NaOH = Na_2SO_3 + C_{10}H_7OH.$$

Sodium naphtalenesulphonate. Naphtol.

The product is purified by pressure, destillation and recrystallization from hot water, or from petroleum ether (from which it separates in scales), to remove all α-naphtol.

Physical and Chemical Properties.—Colorless, lustrous, scaly crystals (or a white crystalline powder), with a faint phenoloid odor, and a transient burning taste; it melts at 123° C., and boils at 286° C. Soluble in alcohol, ether, benzene, chloroform, oils and alkaline liquids. Scarcely soluble in cold, fairly so in hot water (nearly six grains in ℥ j.), forming a liquid which, on the addition of ammonia or soda, exhibits a bluish-violet fluorescence, and on the addition of chlorine water a white turbidity, changed by ammonia to a clear green, and later to brown solution. With ferric chloride the hot aqueous solution gives a green tint (violet if α-naphtol be present), but it is unaffected by ferrous sulphate or lead acetate. In the presence of boric acid a solution of the strength of 1 grain in 2 ounces of lukewarm water may be made (Anotta), which acts more energetically as an antiseptic than either boric acid or naphtol alone.

Inorganic impurities are detected by combustion on platinum foil, and α-naphtol by ferric chloride (*v. supra*). Impure specimens are said to be distinguished by darkening when exposed to light. (*cf.* **Betol.**)

α and β-naphtols are also distinguished by the color formed on melting with 25 times their weight of chloral hydrate; α-naphtol gives an intense ruby-red, not fluorescent, and β-naphtol a pure blue; 40 grains of chloral hydrate and 5 drops of hydrochloric acid dissolve 1½ grains of α-naphtol with an intense, non-transparent, dark greenish-blue color, or the same quantity of β-naphtol to an intense transparent yel-

low (Lustgarten, Reuter). Richardson uses a test solution made by dissolving one grain of *p*-aniline sulphonic acid in water, to which one drachm of normal soda solution had been added; then one drachm of normal sulphuric acid and ⅓ grain of sodium nitrite are also added; the naphtols are dissolved in water containing a few drops of normal soda-lye; *α*-naphtol gives a dark blood-red, and *β*-naphtol a reddish-yellow. By salting out the colors the difference between them is rendered more pronounced. Dilute sulphuric acid does not affect the *β*-color, but changes the *α*-color to dark brown. In the U. S. P. the color reaction with sugar and sulphuric acid is made use of as a distinguishing test. 0.1 gram is mixed with one drop syrup and 5 cc. water, then 3 cc. concentrated sulphuric acid carefully poured down the side of the test-tube to form two distinctive layers; *β*-naphtol gives a yellowish-brown zone, *α*-naphtol a carmine red.

Medicinal Uses.—*β*-naphtol was first introduced into medicine as an antiseptic externally in 1881 (Kaposi). Symptoms of poisoning have been observed after its use (Lesser, Neisser), but these were attributed to impurities in the specimens employed (Shoemaker). An exhaustive pharmacological examination of *β*-naphtol was carried out in 1888 (Willenz), which showed that the compound is not without poisonous effects on animals, though these are less pronounced than some authors believed. It has been employed against skin diseases, organic and parasitic, in ointment form (3 to 10 per cent.), and in alcoholic solution (2 to 10 per cent.). Also in chronic suppurative affections of the middle ear in substance or alcoholic solution (Hand). Internally doses of 5 to 8 grains, several times a day, have been recommended for intestinal disinfection, especially in typhus (Robin and others). In chronic diarrhœa very good results have followed its administration (Ewald).

In 1 per mille solution *β*-naphtol has been highly spoken of as a preservative for anatomical preparations; its powerful bactericidal properties have been established by repeated experiment (Willenz, Bouchard). The *α*- and *β*-naphtols have equal kolyseptic power in preventing the growth of cholera spirillum (Stewart).

DERIVATIVES AND ALLIED COMPOUNDS.

Camphorated β-naphtol is a syrupy liquid, prepared by melting 1 part naphtol with 2 parts camphor, and is used with great success in the antiseptic treatment of boils, coryza, angina diphtheritica, and tuberculosis (Fernet). Against the latter it was given by intraparenchymatous injection in doses of 2 grains mixed with oil. Cures were effected in 21 out of 27 cases of tuberculous glands by emptying any abscess formed, and injecting 7 to 8 drops of camphorated β-naphtol, repeated every two days (Reboul, Nelaton). The pain caused by painting the diseased parts with camphor-naphtol may be alleviated by the addition of cocaine.

Hydronaphtol is an American product, described as a derivative of β-naphtol, obtained by reduction, and put forward as an antiseptic and disinfectant free from the toxic action of the parent compound. As to the actual nature of the substance quite variant opinions have been expressed, and it seems to be still open to doubt, Dr. M. Dockrell has used it against tinea tonsurans in the form of plaster, a chief indication being to prevent the access of air (oxygen). The affected area was shaved, washed with hydronaphtol soap and hot water, covered with over-lapping strips of 10 per cent. hydronaphtol plaster, and the outside margin of the latter painted over with melted hydronaphtol jelly. At the end of four days the plaster was removed and put on fresh. Two repetitions were sufficient to cure (Dockrell). Successfully employed in the treatment of enteric fever and diarrhœa, in doses of two or three grains in capsule, or suspended in milk, every two hours. In typhoid, 3 or even 4 grains were given to begin with every two hours. As it sometimes interfered with digestion, it has been suggested that it might be given in pills coated with keratin (Clarke). Recommended for external use in solution, one part of hydronaphtol dissolved in 10 parts of rectified spirit, to which sufficient glycerin is added to make 1 per cent. solution. In this form the antiseptic properties of the substance were well marked (Bryce).

Microcidin.—This substance, recommended as an antiseptic (Polaillon), is practically sodium naphtol, $C_{10}H_7ONa$, being

prepared by melting β-naphtol with half its weight of sodium hydrate and allowing to cool. A whitish powder is obtained which is soluble in 3 parts of water. For the purposes of wound treatment solutions of 0.3 to 0.5 per cent. of microcidin are recommended; these solutions are non-caustic, non-poisonous, and in activity are ten times as strong as boric acid in the same dilution (Berlioz). In the form of weak solution or ointment microcidin has given good results in the treatment of acute and chronic suppurations of the ear and of all forms of rhinitis, ozaena and tonsilitis (Cozzolini). Microcidin is also recommended for internal use; it reduces febrile temperature and has an antiseptic effect; the greater part is excreted by the kidneys.

Di-iod-β-naphtol, or *Naphtol-aristol.*—An aqueous solution of 2.4 parts each of iodine and iodide of potassium is mixed with a solution of 11 parts of β-naphtol and 4 parts of sodium carbonate; to the mixed liquid a solution of sodium hypochloride is added, when a greenish-yellow substance is thrown down, which is washed and dried in the dark. It is odorless and tasteless, insoluble in water, sparingly taken up by ether, by alcohol or acetic acid, freely so by chloroform; when heated it evolves violet fumes. The preparation is put forward as an antiseptic (Braille), but has not found much employment.

β-naphtol carbonate, $CO(OC_{10}H_7)_2$, the di-naphtyl ester of carbonic acid, is prepared by the action of carbonyl chloride on naphtol-sodium, similarly to guaiacol carbonate. It crystallizes in shining, colorless leaflets, insoluble in water, melting at 176° C., and is readily decomposed into its constituents by weak alkalies. It is recommended as a substitute for β-naphtol for intestinal disinfection, as it is less irritating, but no clinical reports of its use have been published.

Benzonaphtol, or *β-naphtol benzoate*, $C_{10}H_7.OCO.C_6H_5$, analogous to betol (β-naphtol salicylate), is prepared by the action of benzoyl chloride on β-naphtol (equal quantities or an excess of the former) in a sand bath. Reaction begins at 125° C., and at 170° C. is complete in half an hour; it may be expressed as follows:

$$C_6H_5COCl + C_{10}H_7OH = HCl + C_6H_5CO_2C_{10}H_7.$$
Benzoyl chloride. Benzonaphtol.

On cooling the mass crystallizes to a hard cake, from which the benzonaphtol is extracted by boiling alcohol, or the mass broken up into small fragments is digested with twice its weight of a 2 per cent. soda solution and the operation repeated until no further reaction for free naphtol is given (blue color by chloroform and potash).

Benzonaphtol crystallizes in long needles, or forms a white crystalline powder, free from taste and odor, insoluble in water at ordinary temperatures; it melts at 110°. A hot spirituous solution with an equal volume of nitric acid should give no cherry-red color on addition of a few drops of acid mercuric nitrate (free naphtol).

In the intestinal tract the compound is split up into its constituents, and the naphtol remains in the system while the benzoic acid, partly converted into hippuric acid, is excreted with the urine. Given internally to animals it causes diuresis, lowering of temperature, and on cardiac and respiratory action (Dominici). Excellent results were obtained from the experiments on human beings, and the excreted urine was considerably less poisonous than that of β-naphtol (Gilbert). Recommended generally as a disinfectant in diseases of the intestinal tract, from simple diarrhœa to typhoid fever (Yvon, Berlioz, Golbert, Ewald). Of 38 cases of infantile cholera, the remedy was administered with great success in 26 cases, the fœtid odor of stools and feverishness rapidly disappearing, and with negative results in the remainder (Brück). Kuhn failed to find evidence of any antifermentative action. The compound was given in doses of 1¼ drachms (children, 30 grains) *pro die* in frequently repeated small portions, either in powders or emulsion.

Lactol, the lactate of β-naphtol, has recently been recommended as a tasteless and more soluble substitute for Benzonaphtol.

Asaprol, or *β-naphtol-α-mono-sulphonate of calcium*, $[C_{10}H_6(OH)SO_3]_2Ca + 3\ H_2O$, is prepared by saturating the aqueous solution of β-naphtol-sulphonic acid with calcium carbonate, evaporating and crystallizing the salt. Asaprol is

a colorless neutral powder, soluble in 1½ parts of water and in 3 parts of alcohol, and was recommended for therapeutical employment by Stackler and Dubief in 1892. On account of its excellent antipyretic and analgesic action it has found internal employment, especially in France, in numerous diseases, rheumatic disorders, gout, influenza, neuralgias, typhus and the like (Bompart, Dujardin-Beaumetz). It is free from the disadvantages of salicylate of soda (Kern). Though it does not present these disadvantages it does not possess the value of the salicylates in rheumatism, but is to be recommended in cases of epidemic influenza and atonic dyspepsia of the flatulent or acid variety (Wilcox). In doses of 8 grains, given four to eight times a day, in lozenge form or dissolved in tea, coffee or beer. Incompatibles are soluble sulphates, sodium bicarbonate, potassium iodide, antipyrine and quinine.

Naphtopyrin is one of the several phenol compounds of antipyrine experimentally prepared during the past few years. It does not appear to have been yet employed in medicine. Naphtopyrin was made from β-naphtol by prolonged trituration with twice its weight of antipyrine. It forms a tough body, insoluble in water, soluble in alcohol and ether; on keeping for a length of time it slowly assumes a crystalline form.

α-Naphtol, isomeric with the β-compound, is prepared in a similar manner from α-naphtalene-sulphonic acid, the principal product of the action of sulphuric acid on naphtalene at 80° to 90° C. It was recommended in 1888 as an antiseptic of great power and relative harmlessness (Maximowitsch). In solution of 0.1 to 0.25 per mille it acted as a kolyseptic to the spores of the typhoid and tubercle bacillus. In this respect it was one and a half times as strong as β-naphtol but three times less agressive to the skin, etc.; 1½ grains prevented alcoholic fermentatation in a litre of grape sugar solution. According to some authorities (Stewart) it is less poisonous, more soluble and more efficient than β-naphtol, but it proves rather more irritating and therefore the β-form is preferred as a prophylactic, especially as it is less disagreeable in taste. Alpha-naphtol has been administered success-

fully in typhoid fever in 7½ to 15 grain doses, 3 or 4 times a day, together with bismuth salicylate. In acute or chronic affections of the digestive tract it is best administered dissolved in castor oil, whilst inunction with an olive oil solution has proved serviceable in erysipelas, small-pox and other skin diseases (Maximowitsch).

α-Naphtol has been recommended as a test for sugar in urine, the reaction being utilized as follows:—one drop of the urine with 1 drop of a 10 per cent. solution of *α*-naphtol in chloroform is placed in a test tube with 1 ccm. (about 15 min.) of water; concentrated sulphuric acid is then carefully poured in so that the chloroformic solution floats on it. A beautiful violet ring is formed at the surface of contact of the two fluids if only 0.03 per cent. of sugar be present (Molisch and Luther). It is important that *all* the reagents be pure and that the urine be diluted with ten times its volume of water. The reaction is also available for use quantitatively.

α-Oxynaphtoic acid, or *napthol-carboxylic acid*, ($C_{10}H_6OH$-COOH), is obtained by a process analogous to that employed in the preparation of synthetical salicylic acid, viz.: by the action of carbonic acid gas upon sodium *α*-naphtol. It occurs in colorless acicular crystals, with an odor like that of naphtol; m. p. 186° C. This acid is difficultly soluble in cold, more readily in hot water; alcohol and ether take up 10 per cent., and glycerin 0.5 per cent. Forms soluble salts with the alkalies or alkaline carbonates. Recommended as an antiseptic and disinfectant (Ellenberger and Hofmeister, Luebbert), and used in skin diseases and scabies as a ½ per cent. collodion, or with lanolin. Also applied as wool and 10 per cent. ointment (Helbig).

β-oxynaphtoic acid has also been bacteriologically examined and found active.

OREXINE HYDROCHLORIDE.

Synonym : PHENYLDIHYDROCHINAZOLINE HYDROCHLORIDE.

$$C_6H_4 \begin{cases} N\,CH \\ CH_2N\,C_6H_5HCl. \end{cases}$$

A complex derivative of chinoline, first introduced into medicine in 1890.

Preparation.—By the action of metallic sodium on a solution of formanilide (*q. v.*) in benzene, addition of a calculated quantity of o-nitrobenzylchloride, and reduction of the o-nitrobenzylformanilide produced by the action of tin and hydrochloric acid.

Physical and Chemical Properties.—Colorless, or very slightly colored, odorless, lustrous, lanceolate crystals, containing two molecules of water, which effloresce on exposure. Its taste is bitter and pungent, approaching to the caustic, and it is freely soluble in hot water. It powerfully irritates the mucous membrane of the nose.

Medicinal Uses.—Orexine was put forward, in the first instance, as a stomachic of marked activity, exerting simultaneously a stimulant action on the appetite and a tonic influence on the digestive organs (Penzoldt). Being a synthetical remedy that was neither an antipyretic nor an antiseptic, but belonged to an entirely different class of medicaments, orexine attracted a good deal of attention and its literature was rapidly added to. It may be said that the majority of observers more or less strongly corroborated the statements of the original author (Glueckziegel, Hoffmann, Kronfeld, Reichmann, Umpfenbach, Kothar, Boas, Matthes, and recently Gordon and Rizzi), though there have not been wanting others who set less value upon the remedy or altogether denied its usefulness (Imredy, Martius, Podgorski, Battistini, Svirelin). The lack of satisfactory results recorded in some instances has been ascribed to the non-disintegration of the gelatine-coated pills in which it was prescribed. Experiment and clinical observation have shown that such pills may remain in the stomach for hours without being in the least affected. Hence it is recommended to give the remedy in wafers. In doses of 4 to 8 grains it shortens the process of gastric digestion in both healthy persons and patients, producing the more rapid appearance and increase of the hydrochloric acid secretion. It appears to be particularly useful in the anorexia which follows on the shock of major operations, in that of tuberculosis (when not too far advanced), of anæmia and in chronic gastric catarrh. In diseases of the stomach, such as acute catarrh, ulcer and the like, where the

viscus should be protected from irritating agents, it is not suitable. It has been successfully employed by Frommel in alleviating the vomiting of pregnancy, and this is corroborated by others (Graser, Gessner).

In a recent communication, Penzoldt recommends the substitution of the free base, pure orexine, for its hydrochloric acid salt, as being devoid of the burning taste of the latter and causing less tendency to vomit. As the result of prolonged experience with the remedy in over 300 cases of patients suffering from the most various forms of disease, it has proved a valuable stomachic. A dose of 5 grains of the base about ten o'clock in the forenoon appears the best treatment for adults, except where caution is indicated, when a smaller dose (1½ to 3 grains) may be tried. Orexine, however, is very little used at the present time.

As already indicated, orexine should not be prescribed in pill form, but preferably in wafers and accompanied by a copious draught of some liquid (beef-tea, cocoa) in order to prevent any local irritant action.

PARALDEHYDE.

Synonyms: PARALDEHYDUM; ELALDEHYDE.

$$CH_3CH \begin{Bmatrix} OCHCH_3 \\ OCHCH_3 \end{Bmatrix} O.$$

A product of the condensation of three molecules of ordinary ethyl aldehyde.

Preparation.—Ordinary aldehyde is treated at a medium temperature with small quantities of hydrochloric acid, carbon oxychloride, sulphurous anhydride (sulphuric acid causes explosive ebullition), or zinc chloride. The temperature of the liquid rises, and almost complete conversion into paraldehyde occurs. Purification is effected by repeatedly freezing out and rectifying.

Physical and Chemical Properties.—According to the B. P. Additions and U. S. P. (1890) paraldehyde is a clear colorless liquid, having a characteristic ethereal odor, and a burning, and afterwards cooling taste. Specific gravity 0.998.

Boiling point 255.2° F. (124° C.). At 50° F. (10° C.) it begins to congeal to a clear crystalline mass. Miscible in all proportions with rectified spirit or ether. One part dissolves in 10 of water at 60° F. (15.5° C.), forming a neutral solution; it is less soluble in hot water. The requirement that no coloration should be produced when it stands for two hours mixed with a solution of potash or soda, is presumably designed to detect aldehyde if present; freedom from sulphates, chlorides, etc., originating from the method of preparation, is ensured by the statement that neither chloride of barium nor nitrate of silver must produce a precipitate.

It may be pointed out that even pure paraldehyde may be cooled considerably below 10° C. without solidifying unless it be stirred while the temperature is falling. Specimens containing alcohol or aldehyde may remain liquid at —5° C. From a cold saturated aqueous solution containing 11¾ per cent. of paraldehyde about half of the dissolved compound separates at 100° C. Amyl or valer-aldehyde are detected by the odor of the residue left from evaporation of 2 or 3 drachms on the water bath.

As paraldehyde is readily converted into acetic acid by oxidation, and even by the action of atmospheric oxygen, it will not often or long be absolutely neutral. It has, therefore, been provided by the Ph. G. Ed. III. that 1 ccm. with an equal volume of acid-free alcohol should not react acid after the addition of 1 drop of normal potash solution. A more definite limit is given in the U. S. P. It is required that a red coloration shall be produced by the addition of 0.5 ccm. normal potassium hydroxide test solution to a mixture of 8 ccm. paraldehyde and 8 ccm. alcohol containing phenolphthalein.

Medicinal Uses.—Paraldehyde was introduced into medicine about 1883 as a hypnotic and sedative. Physiologically its action is characterized by the absence of action on the heart. It has a strong reducing effect upon the blood, like all aldehydes, and this influence precedes the narcotic action (Froehner). Paraldehyde was specially recommended as a substitute for chloral where this agent was contraindicated or did not produce satisfactory results (Cervello, Krafft-

Ebing). Experiments made quite recently have shown that the presence of paraldehyde, even in minute proportions, accelerates the digestion of fibrin, and that the greater the amount present the more rapid is the digestion, but that the conversion of starch into maltose and dextrine by the pancreatic fluid is retarded (Gordon). It relieves the distressing spasms of idiopathic asthma (Mackie). A paraldehyde habit may be formed (Elkins), but this together with the disagreeable taste are objections that may be overcome; and although it should not be given to individuals predisposed to dyspnœa, owing to its tendency to reduce respiration (Cervello), toxic effects of paraldehyde are very seldom observed, and only in consequence of excessive doses, when they disappear without permanent injury (Friedländer).

Single doses of 40 to 60 min. produce sleep in five to fifteen minutes; half a drachm every three hours produced within half an hour two hours' sleep; 20 min. every four hours for fourteen days produced better sleep at night—not during the day (Therapeutic Committee, Brit. Med. Assoc.). Paraldehyde may be prescribed with tincture of orange or some other bitter tincture; it can also be taken in some form of spirit. An emulsion is prepared by making a thick mucilage with 2 drachms of powdered gum arabic, adding some of the paraldehyde, and having stirred until the mixture is homogeneous, a little water and more paraldehyde are added. One may proceed in this way until as much of the hypnotic has been added as was taken of gum (in this case, therefore, two drachms) making up the mixture to a definite volume (*e. g.*, four ounces) with flavoring agents and water.

The remedy has also been administered in suppositories and subcutaneously, but there is seldom need to resort to these forms as it is promptly absorbed from the stomach.

DERIVATIVES AND ALLIED COMPOUNDS.

Metaldehyde [$(C_2H_4O)_n$] is formed by the action of polymerising agents upon aldehyde at a temperature below 0° C. It is a white crystalline body, insoluble in water, but freely taken up by hot alcohol and ether. When heated it sublimes without melting between 112° to 115° C., being at the same

time partially decomposed. Metaldehyde has been credited with hypnotic properties.

Sulphaldehyde was described in the early part of 1891 as obtained by the action of sulphuretted hydrogen upon ordinary aldehyde. It forms, according to the note published, an oily liquid with a repulsive odor, solidifying at —8°, and melting again at —2° C. Treated with acid it seems to undergo polymerisation, like aldehyde, forming the solid sulpho-, or thio-paraldehyde. According to Luisini sulphaldehyde produced a deep and quiet sleep in frogs and rabbits, and proved more powerful than paraldehyde: ⅙ min. producing the same effect as nearly ½ min. of the lattor. Luisini's recommendation does not seem to have at all attracted attention, at least nothing further has appeared.

PENTAL.

Synonyms: TRIMETHYLETHYLENE; *β*-ISOAMYLENE.

$(CH_3)_2C.CH.CH_3$.

An impure amylene was described in 1844 (Balard) and used in 1856—1857, after which it fell into oblivion.

Preparation.—Amyl alcohol produced by fermentation, is distilled with zinc chloride; ordinary amylene is obtained which consists of trimethylethylene (about 50 per cent.) with pentane, C_5H_{12}, (boiling at 29° C.), together with varying quantities of *α*- and *γ*-amylene. If shaken in the cold (—20° C.) with sulphuric acid which is diluted with ½ to 1 volume of water, the trimethylethylene dissolves (as also does any *γ*-amylene present) to amyl-sulphuric acid, which after dilution with water yields on distillation pure trimethylethylene and tertiary amyl alcohol. From the latter the pental is separated by fractional distillation. Also obtained from amylene hydrate by the action of acids.

Physical and Chemical Properties.—A colorless liquid, of low specific gravity (0.62), insoluble in water, but miscible in all proportions with alcohol, chloroform or ether. Pental boils at 38° C., and the vapor is highly inflammable; being characterized by considerable stability it does not decompose on exposure to light and air.

Medicinal Uses.—Pental was introduced towards the close of 1891 as an anæsthetic especially suitable for use in dental surgery. The narcosis sets in after 1 to 1½ minutes, although, of course, this times varies, according to the character of the patients, being shorter when they are quiet and breathe regularly. The anæsthesia appears to be complete before consciousness is altogether lost, and the awakening is quite gradual. Neither during the narcosis nor afterwards are any unpleasant symptoms observed (Hollænder, von Mering, Weber, Mebes, von Rogner). Over ethyl bromide, the chief liquid anæsthetic in use, it seems to have the advantage of greater stability and freedom from irritant effects; it never produces the cramp-like spasms of the bromide (Hollænder). Some recent investigators consider pental as unsafe; and anyhow several cases of collapse and death during pental narcosis must be a warning for the greatest care in administration (Cerna, Breuer and Lindner, Haegler). In 5 cases it caused albuminuria (Kleindienst). On the other hand some operators consider it the best anæsthetic in short operations (Bauchwitz), whilst Hollænder reports that he has now employed pental successfully in 1200 narcoses, and Feodoroff has used it in 117 minor operations and Velez in 108 cases with very gratifying results.

Pental is best administered by the apparatus known as Junker's (which is provided with an India-rubber ball for forcing air through the liquid), but for quite short operations a well-fitting chloroform mask (Skinner or Esmarch) may be made available for the purpose by covering it with a few folds of flannel and finally with some impermeable material; 2 to 3 drachms of pental are generally sufficient to produce satisfactory narcosis for ordinary operations.

PHENACETINE.

Synonyms: PHENACETINUM; ACETPHENETIDINE.

$C_6H_4OC_2H_5NHCH_3CO$.

A crystalline compound closely allied in chemical constitution to acetanilide and methacetine.

Preparation.—Sodium para-nitrophenol (*v.* Preparation of **Methacetine**) is converted by the action of ethyl iodide into *p*-nitrophenetol, the latter reduced to *p*-amidophenetol (*p*-phenetidine), which by prolonged boiling with glacial acetic acid yields phenacetine. The equations are (*v.* also **Methacetine**):—

$$\underset{\text{Sodium } p\text{-nitrophenol.}}{C_6H_4ONaNO_2} + C_2H_5I = NaI + \underset{p\text{-Nitrophenetol.}}{C_6H_4OC_2H_5NO_2}$$

$$C_6H_4OC_2H_5NO_2 + 6\ H = 2\ H_2O + \underset{p\text{-Phenetidine.}}{C_6H_4OC_2H_5NH_2}$$

$$C_6H_4OC_2H_5NH_2 + CH_3COOH = H_2O + \underset{\text{Phenacetine.}}{C_6H_4OC_2H_5NHCH_3CO.}$$

Physical and Chemical Properties.—The B. P. Addendum describes phenacetine as occuring in colorless, tasteless, inodorous, glistening, scaly crystals, melting at 275° F. (135° C.), sparingly soluble in cold, more freely in boiling water (1:70, Ph. G.) and in about 16 fluid parts of rect. spirit. A lower melting point observed in some preparations has been thought to be due to the presence of di-acetphenetidine (Thoms), and it is at any rate an indication of impurity.

Phenacetine is officially identified by the production of a deep red color when chromic acid is added to a cooled and filtered solution of 1 grain in 20 minims of hydrochloric acid diluted with ten times its volume of water (Ritsert). Its freedom from acetanilide is indicated by the absence of turbidity on addition of bromine water to a cold saturated aqueous solution. The isonitrile test for freedom of phenacetine from acetanilide must be made with caution, as by continued heating of phenacetine with alkalies, *p*-amidophenetol is split off and yields the isonitrile reaction. Lastly, sulphuric acid must dissolve it without color; and heated with free access of air "it burns leaving no residue."

The method of dlstinguishing phenacetine from similarly constituted bodies is described under **Exalgine, Acetanilide,** and **Methacetine** (*q. v.*). Like the two latter, acet-*p*.-phenetidine gives the indophenol reaction. For the detection of 2 or more per cent. of acetanilide in phenacetine, Schroeder recommended boiling 8 grains with about 15 minims of water, cooling, filtering, boiling the filtrate with nitrous acid

(or a mixture of potassium nitrite and dilute nitric acid), adding a few drops of Plugge's reagent (a solution of mercurous nitrate containing nitrous acid), and boiling again. In the presence of two or more per cent. of acetanilide the liquid assumes a red color, due to the production of an azo dye.

A later test consists in covering finely powdered phenacetine with 10 to 12 per cent. nitric acid, and heating to boiling; an intense yellow nitro compound is formed, and on cooling partly separates in yellow needles. Antipyrine and acetanilide are unaffected under the same conditions (Autenrieth and Hinsberg); but this test is not reliable or conclusive by itself.

When 40 grains of chloral hydrate are melted in a water bath, 8 grains of phenacetine added, and the whole shaken together, solution occurs which in the presence of only traces of paraphenetidine is colored immediately violet, reddish or bluish in tint, according to the proportion of the impurity present (Reuter).

Further, phenacetine, free from phenetidine, which, under the same conditions, remains colorless, even when warmed, for at least five minutes, gives a pink-colored solution after prolonged digestion (identity). A less delicate test is a dilute aqueous iodine solution (1:20,000); 8 grains of phenacetine are shaken with 1½ drachms of this solution, and the liquid filtered; a pure compound yields a colorless filtrate (a pink tint = paraphenetidine). Goldmann uses a solution of 8 grains of phenacetine in ½ drachm of spirit; to this the 1½ drachms of iodine solution is added, and the liquid, with the separated phenacetine, boiled till solution is effected, which is pink if traces of *p.*-phenetidine be present.

Medicinal Uses.—Phenacetine was first recommended as an antifebrile for use in medicine in 1887 (Hinsberg and Kast), since when its literature has attained large dimensions. It has been given in phthisis, typhus, polyarthritis (Collischonn, Rifat), peritonitis, endocarditis, abdominal typhus (Kartschewski), etc., with success, and has also made a reputation as an antineuralgic in vasomotor neuroses in the lancinating pains of tabes of neuralgia and hemicrania (Kobler, Hoppe, Guttmann, Lépine, Dujardin-Beaumetz, Mueller, Mahnert, and others). Success followed its use in

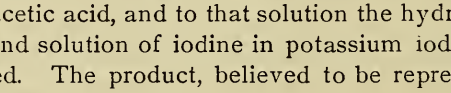
the whooping cough of children (Michaelis, Kratz, Heimann, Irwin), and in epidemic influenza both as a prophylactic and remedy (Wolff, Rathgen, Hallam, Cleveland, Weed, Henry).

The action of phenacetine seems to be free from collapse and unpleasant by-effects generally; like most of the synthetical antipyretics its antifebrile effects are accompanied by more or less profuse perspiration. When fever is accompanied by unrest, sleeplessness, etc., phenacetine has been found to reduce the high temperature and produce quiet sleep without being followed by headache.

The dose as an antipyretic is 8 to 12 grains hourly, or every two hours, as may be necessary. As an antineuralgic and against rheumatism 15 grains are given, repeated if required until 1½ drachms have been taken in the twenty-four hours. It has been given with benefit in 2 grain doses combined with 12 grains of caffeine against migraine Best prescribed and dispensed in powders or readily disintegrating tablets.

DERIVATIVES AND ALLIED COMPOUNDS.

Iodophenine, or *Iodophenacetine.*—If to a cold saturated aqueous solution of phenacetine, a solution of iodine in potassium iodide, or bromine water be added, or if chlorine be led in to saturation, brown, yellow or greenish solutions are obtained which also remain clear on long standing. It is, however, otherwise if to these solutions hydrochloric acid be added, or if the acid be added before the halogen; under these conditions iodine yields an abundant precipitate. For preparation on a large scale the phenacetine is dissolved in glacial acetic acid, and to that solution the hydrochloric acid, water, and solution of iodine in potassium iodide and water are added. The product, believed to be represented by the formula:—



occurs in fine crystals similar in form to those of potassium permanganate; it has a feeble iodine-like odor, a coarse burning taste, and colors the skin yellow. M. p. 130° to 131°

with decomposition. Soluble in glacial acetic acid, boiling hydrochloric acid, and in alcohol. Heated or even simply mixed with water, iodine is set free (Siebel).

Owing to the looseness with which iodine (about 50 per cent.) is held in the compound it exerts marked antiseptic properties (Wittkowsky), and, indeed, has the irritating effects of free iodine (Siebel). For the latter reason it has been said to have no advantages over pure iodine, and it has at any rate not come into therapeutical use.

Methyl phenacetine, $C_6H_4(OC_2H_5)N(CH_3)CH_3CO$.—Prepared by the action of methyl iodide on phenacetine-sodium in solution in xylene. Colorless crystals, melting at 40° C., sparingly soluble in water, easily in alcohol and ether. It is said to have a hypnotic action, but no clinical reports have yet appeared.

Ethyl-phenacetine, $C_6H_4(OC_2H_5)N(C_2H_5)CH_3CO$.—The homologue of the above preparation and obtained in the same manner by the action of ethyl iodide on phenacetine-sodium. A yellowish oil, boiling at 330° to 335°, and solidifying on cooling; also possesses hypnotic properties, but to a lower degree than the methyl derivative.

Formyl-phenetidine, or *para-ethoxy-formanilide*, $C_6H_4(OC_2H_5)NH.COH$, is the simplest homologue of phenacetine, and is prepared by the action of formic acid and anhydrous sodium formate on phenetidine hydrochloride. Colorless, tasteless, and odorless crystals, melting at 60° C., slightly soluble in cold water, easily soluble in hot water, alcohol and ether. It is said to have an antispastic action, but no clinical reports have been published.

Lactophenine, or *lactyl-phenetidine*, obtained by the interaction of lactic acid and phenetidine in the presence of dehydrating agents, is recommended as a substitute for phenacetine on account of its greater solubility. It is a crystalline powder, of slightly bitter and not unpleasant taste, possessing an antipyretic and sedative action, and especially indicated in abdominal typhus—where is has been employed with success (Jaksch). It is best administered in wafer form, in doses of 8 to 15 grains, up to 1½ drachms daily.

Sedatin, or *valeryl-phenetidine*, is the product of the action

of valerianic acid on para-amido-phenetol. It is a crystalline body, boiling at 350 to 360° C., and comparatively insoluble in ordinary reagents. It is said to have a pronounced sedative and antineuralgic effect, but no clinical reports of its action have appeared. The term sedatin was formerly used as a synonym for antipyrine (*q. v.*).

Salicyl-, *Benzoyl-*, and *Anisyl-phenetidine.*—These derivatives of phenetidine are obtained by the action of the respective acids upon the base in the presence of phosphorous chloride or phosphoric oxychloride; their formulæ correspond exactly to that of phenacetine with the groups $CO.C_6H_4.OH$, COC_6H_5 and $CO.C_6H_4.OCH_3$ respectively replacing CH_3CO. All three are physiologically inert, in consonance with the indications of recent research showing that the introduction of aromatic acid groups into the molecule of the synthetical antifebriles deprives them of their antipyretic virtues (Ehrlich, Aronson). Although the first named, under the abbreviated title "saliphen"—not to be confounded with salophen (*q. v.*)—was introduced in 1890, none of the compounds have achieved more than a scientific interest.

Thymacetin.—This is another substance closely allied to phenacetine, but derived from thymol instead of from benzene, and represented by the formula:—

$$\begin{matrix} CH_3 \\ C_3H_7 \end{matrix}\!\!\diagdown\!\!\diagup C_6H_2 \!\!\begin{matrix} \diagup OC_2H_5 \\ \diagdown NH(CH_3CO). \end{matrix}$$

It occurs as a white crystalline powder, melts at 136° C., and dissolves with difficulty in water, more easily in alcohol and ether. It is said to act as a hypnotic in doses of 5 to 45 grains, and to be, so far as present experiments go, without toxic action on warm-blooded animals. It has been employed in neuralgia (Jolly), but is said to produce dizziness and other unpleasant head-symptoms, and is neither analgesic nor hypnotic (de Montyel).

Iatrol, an American product, is said to be an oxy-ethoxy-anilide; but the published formula, $NH.C_6H_5O_2(C_2H_5O)I_2$, gives no clue to its character. It is described as an absolutely odorless and non-poisonous powder, excelling iodoform in its action; but in the absence of more definite information no importance can be attached to it.

PHENOCOLL HYDROCHLORIDE.

Synonym: GLYCOCOLL-PHENETIDINE HYDROCHLORIDE.

$$C_6H_4\begin{cases}OC_2H_5\\NHCO.CH_2NH_2HCl.\end{cases}$$

One of the latest additions to the numerous class of antipyretics, distinguished by its comparatively free solubility; is chemically closely related to phenacetine.

Preparation.—By the interaction of phenetidine (paraamidophenetol) and glycocoll or amidoacetic acid esters. The reaction may be expressed by the following equation :—

$$\underset{\text{Phenetidine.}}{C_6H_4(OC_2H_5)(NH_2)} + HOOCCH_2NH_2 = \underset{\text{Phenocoll.}}{C_6H_4(OC_2H_5)(NH.COCH_2NH_2)} + H_2O$$

Also prepared by the action of chloracetylchloride on phenetidine and subsequent treatment with ammonia.

The possibility of forming salts is due to the presence of the second amide group.

Physical and Chemical Properties.—Phenocoll hydrochloride occurs in the form of a white micro-crystalline powder, soluble at 17° C. in about 16 parts of water, and forming a neutral solution. From hot water it crystallizes in cubes similarly to antipyrine, and from alcohol, in which it is only freely soluble when heated, in needles. Ammonia, the fixed alkalies, and their carbonates throw down the pure base, from a solution of the hydrochloride, in the form of white-matted needles, with one molecule of water of crystallization.

The anhydrous base melts at 100 5° C., but the compound with water at 95° C. Phenocoll is very difficultly soluble in cold, but readily in hot water; it is freely taken up by alcohol, but very little by ether, benzene and chloroform. Dilute solutions of the alkalies and their carbonates, and dilute acids, even though boiling, do not readily decompose the base; after prolonged treatment in this way it partially splits up into phenetidine and glycocoll.

The solution of 1 part phenocoll hydrochloride in 30 parts distilled water is clear (turbidity indicates the presence of

di- or tri-phenocoll), and not colored ether in cold or warm by ferric chloride (absence of phenetidine). On addition of caustic soda to the warm solution no ammonia should be evolved, but the base precipitated of a pure white color (colorations indicate impurities). No residue is left by incineration on platinum foil.

Medicinal Uses.—The difficulty referred to in a previous monograph (*v.* Salicyl-phenetidine) of preparing soluble antipyretics by the introduction of acid groups, was overcome in the case of phenocoll by the substitution of a basic group, viz., that of glycocoll. Physiologically the compound appears to have a marked advantage over nearly all synthetical antipyretics of the aromatic series, in that it has no injurious effect upon the blood corpuscles even when directly brought into contact with them (Kobert, von Mering, Cerna and Carter, Balzer). It has an effect upon the respiratory centres (Ott). As would be expected from this fact the action of the compound has proved safe, (except in the case of emaciated consumptives) and without unpleasant by-effects; albumen has not been observed in the urine of patients. Satisfactory results are recorded from its employment as an antifebrile in phthisis and other pulmonary affections, in ileotyphus, etc. (Herzog, von Mering, Hertel, Jacobi, Cohnheim), as an antirheumatic especially in acute forms (Hertel, Cohnheim), and as an antineuralgic (Herzog, Aronson, Cohnheim).

Recently phenocoll has come into quite extensive use as a specific in malarial affections, and Italian observers especially have given it great attention. It is not an antimalaricum in the sense of developing antiparasitic action on plasmodia, but it exercises a beneficent effect upon the febrile and other conditions accompanying the malady, and is devoid of any tendency to abnormal lowering of the temperature (Colosanti and Geronzi, Albertoni, Mosso, Golgi, and others). In 18 cases of quotidian, tertian and erratic forms of malaria, 15 cures were effected (Cervello), and of 84 cases in Castelbuono in only 4 was it without effect. It is considered by some as a veritable substitute for quinine; it does not cause singing in the ears, cutaneous eruptions or other toxic symptoms, as quinine is apt to do, and as its taste is not difficult to mask it

is readily administered to children (Dall'Olio). Similar reports have also been received from malarial districts in America (Cerna). Owing to its value as an intestinal antiseptic as well as an antipyretic, phenocoll is especially indicated in typhoid and typhus fevers (Egbert).

Given in 8 grain doses when the febrile temperature fluctuates between 30° and 40.5°, a reduction of about 2° is obtained, accompanied by more or less profuse perspiration; in isolated cases a dose of 8 grains has been followed by a fall of 4° (Cohnheim). In neuralgia small single doses are not so effective as 8 grains three times a day; phenocoll is not indicated in cases of hysterical origin. In acute rheumatism the same single dose was ordered three to seven times a day; a very rapid effect was produced upon the pain and swelling.

Phenocoll hydrochloride may be prescribed as powder, in capsules, or merely in aqueous solution (ʒ j : ʒ iv.) with or without correctives. Patients do not complain of the slightly bitter taste of the remedy.

Phenocoll hydrochloride has also been recommended as an antiseptic in the treatmeat of wounds, open sores, etc., either in powder form, in 5 per cent. aqueous solution, 10 and 15 per cent. alcoholic solutions, 10 and 20 per cent. gauze, and 10 and 20 per cent. lanolin and vaseline ointments (Beck). It is said to be fully as efficient as iodoform, and has the advantage of inodorousness, solubility, and absence of irritant and toxic effects, enabling it to be spread over large surfaces in considerable quantities, and further it is not contra-indicated in kidney affections.

DERIVATIVES AND ALLIED COMPOUNDS.

Salocoll, or *Phenocoll-salicylate*, is the only other salt of phenocoll that has been therapeutically employed. It is rather less soluble (1 : 200) than the hydrochloride, but forms neutral solutions of sweetish taste, that give a violet coloration with ferric chloride. It combines the therapeutical action of phenocoll with that of salicylic acid, and is therefore indicated as a reliable and safe antipyretic and antirheumatic, which in practical experience is reported free from gastric

disturbance and untoward effects. It is given in doses of 15 grains for adults several times daily in powder form.

Other salts of phenocoll have also been described, but so far have not been therapeutically employed. The *carbonate* is an almost tasteless, bulky powder, readily dissolved by weak acids. An *acetate*, soluble in 3½ parts of water, is also known and appears suitable for subcutaneous injection.

PIPERAZINE.

Synonyms: Piperazidine; Ethylenimine; Diethylendiamine; Dispermine.

$C_4H_{10}N_2$.

A synthetical compound primarily intended to replace spermine, but found to be a different body in both chemical and physiological characters.

Preparation.—Piperazine has been formed from the action of ammonia on ethylene bromide or chloride. In this way the salts of a mixture of bases is obtained, consisting of ethylene diamine, a proportion of high-boiling bases such as triethylene diamine, diethylene triamine, tetrethylene triamine, and of a small quantity of diethylene diamine. The mixture of bases fractionated, yields a fraction between 130° and 180° C., from which on cooling the diethylene diamine may be separated (Hofmann), but more easily by adding sodium nitrite to the mixture, whereupon dinitrosopiperazine crystallizes out and yields free piperazine by distillation with alkalies.

Various complicated processes have been patented for the manufacture of piperazine, which is impracticable by the above methods. The most important of these effect the more regular formation of aromatic derivatives of piperazine, as diphenylpiperazine, by the interaction of aniline and ethylene bromide, from which piperazine is subsequently obtained by treatment with nitrous or sulphuric acids and distillation of the resulting products with alkalies or alkaline sulphites.

$$2\ C_6H_5.NH_2 + 2\ C_2H_4Br_2 = C_6H_5.N\begin{matrix}<CH_2.CH_2\\ <CH_2.CH_2\end{matrix}>N.C_6H_5 + 2\ HBr.$$

Aniline. Ethylene Bromide. Diphenylpiperazine.

$$C_6H_5.N(C_4H_8)N.C_6H_5 + 2HNO_2 = NO.C_6H_4.N(C_4H_8)N.C_6H_4.NO + 2\ H_2O.$$

Nitrous Acid. Dinitrosodiphenylpiperazine.

$$NO.C_6H_4.N(C_4H_8)N.C_6H_4.NO + 2\ H_2O = NH\begin{matrix}<CH_2.CH_2\\ <CH_2.CH_2\end{matrix}>NH + 2\ C_6H_4(OH)NO.$$

Piperazine. Nitrosophenol.

A synthetical process more easily represented is the reduction of ethylene oxamide to piperazine with nascent hydrogen:

$$\begin{matrix}CH_2-NH-CO\\ |\qquad\quad |\\ CH_2-NH-CO\end{matrix} + 4\ H_2 = \begin{matrix}CH_2-NH-CH_2\\ |\qquad\quad |\\ CH_2-NH-CH_2\end{matrix} + 2\ H_2O$$

Ethylene oxamide. Piperazine.

Physical and Chemical Properties.—Piperazine is solid; it melts at 104° to 107° C., and boils at 145°. It is extraordinarily readily soluble in water, and can therefore be applied subcutaneously. Crystallized from water it forms glassy, lustrous tables, and can be obtained both in anhydrous condition and in form of various hydrates. From the air it greedily absorbs water and carbon dioxide, and liquifies in so doing. The aqueous solution is almost tasteless, and has a strongly alkaline, but non-caustic reaction.

The hydrochloride of piperazine is also very easily soluble in water, more difficultly in alcohol; it crystallizes in silky, lustrous, lanceolate forms.

The base is unaffected by aqueous chromic acid, or by fuming sulphuric acid, even if heated to 110°; permanganate gradually oxidizes the base in the cold.

The aqueous solution of piperazine gives a white precipitate with Nessler's reagent and with mercuric chloride; a blue precipitate with copper sulphate, insoluble in excess; and a lemon-yellow crystalline precipitate with picric acid, soluble in hot water. In not too dilute solutions in dilute hydrochloride acid, a bright yellow, crystalline gold salt is produced.

The most characteristic reaction of piperazine is, however, the pomegranate-red precipitate produced by potassium bismuth-iodide solution in dilute hydrochloric acid solutions of the base. This precipitate is so insoluble that it may be employed for quantitative estimation as well as for qualitative detection of piperazine.

Piperazine may be detected in the urine, by adding a few drops of concentrated soda to about 100 ccm. (3½ fl. ozs.) of the excretion, warming gently for a short time, allowing to cool, filtering (from phosphates, etc.), making decidedly but not too acid with a few drops of hydrochloric acid, and adding potassium-bismuth-iodide solution. First of all a discolored amorphous precipitate of a compound with the nucleo-albumen of normal urine is formed; this contains no piperazine. The whole is warmed for a short time to 40 to 50°, whereby the precipitate aggregates, then rapidly cooled and filtered; on energetically stirring with the glass rod, the bismuth-piperazine compound crystallizes out gradually, and falls as a fine pomegranate-red powder, the stellate crystalline form of which may be readily identified under the microscope (Majert and Schmidt)

An additional characteristic reaction of piperazine is the ready formation of a benzoyl derivative on addition of benzoylchloride to an alkaline solution of piperazine. Dibenzoylpiperazine crystallizes out of alcohol in rhombic tablets, melting at 191° C.

The most valuable chemical property of piperazine is its power of forming a readily soluble compound with uric acid; this character is possessed to a more or less extent by other organic bases of similar composition, the active physiological or toxic properties of which, however, prevent their therapeutical application. * If brought together in cold aqueous solution with uric acid it dissolves 12 times as much as will carbonate of lithium under the same conditions, and the piperazine urate formed is seven times more soluble in water

* It is noteworthy that, according to Professor R. Kobert, *Cadaverine*, $C_5H_{14}N_2$—a ptomaine with some chemical relationship to piperazine—possesses the same property of forming a relatively readily soluble urate.

at 17° C. than urate of lithium. One part of the latter requires 368 parts of water for solution, while one part of piperazine urate is taken up by 50 parts of water (Biesenthal and Schmidt). Even when an excess of the acid is present only the readily soluble neutral salt is formed under normal conditions, and an acid urate formed in hot concentrated solutions is decomposed by water into the neutral urate and free acid; the solvent action of piperazine on both uric acid and acid urate of sodium, is developed in aqueous solution even in the dilution of 1 to 4000, but its action on uric acid suspended in urine is diminished (Helbing and Passmore). In weak or strong solutions in urine, however, piperazine converts the undissolved portions of the calculus into a soft granular or pulpy condition, which neither borax, lithium citrate, sodium carbonate, or potassium citrate are able to do under similar conditions. Its solvent action is also greater than that of any of these substances, and although the stronger the solution of piperazine in urine, the earlier did the solvent action begin and the more rapid was its completion, the rate of solubility was not so markedly rapid in the stronger over the weaker solutions as might be expected (Gordon).

Medicinal Uses.—It was at first anticipated that piperazine would display nervine and stimulant properties similar to those ascribed to "spermine" (Brown-Séquard, Poehl and others), the active principle of which was believed to be a body of the same constitution. Physiological experiment and chemical investigation showed that this was not the case; the compound appeared to be practically inert, and certainly without powerful physiological effect (Kobert, Bock). Consideration of the behavior of the base with uric acid suggested its employment in the affections characteristic of the gouty diathesis. Earlier researches on the effect of the administration of piperazine upon metastasis was believed to indicate the fact that the amount of urea increased while that of the uric acid decreased (Vogt, Vigier and Gautrelot). This conclusion, however, was not confirmed by later observers. The compound was tried with fairly encouraging results in mental diseases (Umpfenbach, Peretti, Schultze), but by far the greater share of attention has been

concentrated upon its uric acid solvent properties. It is very well borne without any ill results even when given for prolonged periods (Ebstein, Sprague and others), and exerts a marked solvent action upon concretions of urates and gouty tophi (Bardet). This latter property has been tested in the laboratory (Holtz) and practically evidenced in the clinical treatment of cases (Heubach and Kuh, Krakauer, Brik, Biesenthal and Schmidt). In 15 grain doses daily the use of piperazine in gout has been promptly followed by reduction of redness and swelling of the affected joints, while a general feeling of well-being set in; very frequently the administration of the remedy is followed by a discharge of gravel. As a solvent for uric acid and urate concretions it is far superior to all known medicaments (Biesenthal and Schmidt), but as these solvent properties are not developed in urinary so well as in aqueous menstrua, its real character as a solvent of uric acid in the organism has been disputed (Mendelsohn, Bohland).

In the past two years its therapeutical employment has however certainly increased. No less than 150 cases of gout have been successfully treated, and large gouty concretions in elbows, ears and eyelids removed by combined internal and subcutaneous administration, by Schwenninger. Other authors (von Hergel, Ritter, Volmer, Pfeiffer, Stewart, Hamilton) have employed piperazine successfully in renal colic, gravel and stone, as well as in gouty disorders. Its beneficial action is specially marked in hereditary gout and uric acid diathesis (Barbour). Artificial deposits in the animal organism produced by injections of chromic acid were dissolved or avoided by administration of piperazine (Meisels, Biesenthal). The employment of piperazine, owing to its solvent action on the binding action of concretions has also been suggested in sclerosis, rheumatic arthritis, and other disorders accompanied by deposits in the system (Finzelberg), and in arthritis has so far been favorably reported upon (Ritter, Volmer, Wittzack, Bullard). Marked relief has also been afforded by the remedy in the itching of pruritus (Disbrow), and it has lately been recommended in diabetes (Hildebrand, Gruber).

Being without caustic action upon the mucous membrane, solutions of piperazine may be directly introduced into the bladder in order to dissolve vesical stones; and by virtue of its solubility and non-irritating properties it is suitable for local subcutaneous administration in gout. A solution (1 to 2 per cent.) in a mixture of water and spirit (1:4 respectively) has been recommended for topical application by means of the Priessnitz compress.

Piperazine is readily absorbed from the stomach and passes through the organism without suffering dissociation or resolution. Circulating with the blood unchanged, it is believed to reach the areas affected by gouty deposits in a condition in which it is readily able to neutralize and dissolve them and thus facilitate their removal from the body. Comparative experiments have also been made upon the diffusibility of piperazine, sodium and lithium urates, through animal membrane, which established the superiority of the first named (Biesenthal and Schmidt).

The administration of piperazine has been remarkably free from bye-effects on the system owing to the stability of the base in the organism. Other than an instance of urticaria arising after the administration of piperazine (Bradford), no deleterious effect has been noted except an alleged occurrence of albuimnuria (Roerig) which has been disproved, the fallacy arising from mistaking the precipitate given with picric acid in urine containing piperazine for an indication of albumen (Biesenthal).

Piperazine, given in doses of 15 grains daily, should be dissolved in about 1 pint of water. A combination of phenocoll and piperazine in solution with plain or aërated water—15 grains of each per pint, dissolved separately and the solutions poured together—is specially recommended as an effective and agreeable form of taking the remedy. In the proportion indicated it does not affect the taste of the water, and has been successfully used in practice.

DERIVATIVES AND ALLIED COMPOUNDS.

Lycetol, or *dimethyl-piperazine tartrate*, has recently been introduced as a substitute for piperazine. It is prepared by the

distillation of glycerin with ammonium chloride or bromide, and reduction of the dimethylpyrazine isolated from the distillation products with sodium in alcoholic solution. The free base, dimethyl-piperazine, is a crystalline substance, melting at 118° C., and readily volatilized. It is very soluble in water, yielding alkaline solutions that readily dissolve uric acid. The latter property is also shared by the tartrate, Lycetol, which is an anhydrous salt, consisting of a small granular powder, easily soluble in water, but only slightly hygroscopic. It has been administered in 7 cases of gout with good effect, and is also said to have a diuretic action (Wittzack), but nothing as regards dosage has yet been published, though probably it is the same as that of piperazine. A salicylic acid salt of the base is less soluble in water and has a slighter solvent action on uric acid (Oefele).

Diacetyl-piperazine, $C_4H_8N_2.2C_2H_3O$, is the product of the action of excess of acetic anhydride upon piperazine acetate under a return condenser; m. p. 138.5°. By the action of *p*-chlornitrobenzene upon piperazine *β-nitrophenyl-piperazine*, melting at 129°, is obtained. A dinitro-product is yielded if excess of the chlornitrobenzol be employed. Other derivatives have also been obtained, but it does not seem intended to introduce them into medicine.

Tetra-ethylammonium hydroxide, $(C_2H_5)_4N.OH$, has also been recommended as a solvent for uric acid. It is readily soluble in water, yielding bitter, alkaline, caustic solutions. Administered internally in doses of 8 to 15 minims of a 10 per cent. solution, three or four times daily (Petersen).

Uricedin, a so-called "synthetic" salt, introduced for the treatment of gout, consists of a mixture of citrates and sulphates of alkalies, principally of sodium to a small proportion of lithium, in which chlorides and carbonates have also been found.

PYRIDINE.

C_5H_5N.

A liquid body formerly regarded as constitutionally analogous to chinoline, but recently stated to exhibit differences in behavior so important that the nitrogen atom is

believed to occupy a different position in the molecules of the two compounds.

Preparation.—From coal-tar oil and bone-oil, by treatment with sulphuric acid, separation of the sulphonic compounds and decomposition with soda. The mixture of bases set free (pyridine, anilines, etc.), is carefully fractionated, the distillate treated with acid oxidizing agents (which attack only the aniline bases), neutralized with soda, and fractionated again. Small quantities of very pure pyridine are obtained by distilling calcium nicotate with lime, thus :—

$$(C_5H_4NCOO)_2Ca + Ca(OH)_2 = 2\ CaCo_3 + C_5H_5N.$$

Calcium nicotate. Pyridine.

Physical and Chemical Properties.—Pure pyridine is a colorless liquid, with a peculiar empyreumatic odor and a pungent taste; specific gravity 0.98° at 15° C.; boiling point 117° C. Miscible with water in all proportions, and considerably hygroscopic. Pyridine forms salts with acids by direct addition, like the alkaloids, of many of which, as known, it is regarded as the parent substance. It is distinguished from aniline bases in its power of resisting the action of oxidizing agents.

Pyridine should not be altered by exposure to light; it should not contain ammonia (as evidenced by absence of reddening on the addition of phenolphtalein to the 10 per cent. aqueous solution), and two drachms of the same aqueous solution to which three drops of volumetric permanganate solution have been added should maintain the red color for at least an hour (absence of readily oxidizable compounds).

Medicinal Uses.—Internally pyridine has been given pure—3 to 4 drops three times a day—as a stimulant in cardiac diseases. Against diphtheria it has been locally applied, a 10 per cent. aqueous solution or a mixture of pyridine and peppermint oil being painted on the affected parts.

Pyridine bases are well known to occur in tobacco smoke, which has frequently proved beneficial in asthma; its use has therefore been recommended for the relief of asthmatic troubles (Germain Sée). From 1 to 1½ drachms are poured on a plate and placed in the room with the patients. In a

temperature of 68° to 77° F., the above named quantity is evaporated in about an hour. It is said that after a few minutes of exposure to the pyridine atmosphere the remedy can be detected in the urine. The treatment was well-spoken of (Kelemen), but does not seem to have maintained its ground. In aqueous solution (1 : 300) 3 or 4 injections have been said to be sufficient to cure gonorrhœa (Rademacher), but this statement has not been confirmed by others (Wollenberg). It must be borne in mind that pyridine is a strongly alkaline irritant poison in quantity (Catani); a fatal case of poisoning was recently recorded from swallowing "half-a-cupful" of commercial pyridine (Helme).

RESORCIN.

Synonym: Metadihydroxybenzene.

$C_6H_4(OH)_2$.

A compound primarily prepared in 1864 by Barth and Hlasiwetz from umbelliferous resins by fusing with potash.

Preparation.—By converting benzene into benzene disulphonic acid, neutralization with milk of lime, decomposition with soda, filtration (to remove the chalk formed), and evaporation to dryness. The product (sodium *m*-benzenedisulphonate) is fused with caustic soda for eight or nine hours, the mixture allowed to cool, dissolved in boiling water, hydrochloric acid added, the boiling continued till all the sulphurous anhydride has escaped. On cooling the mass is filtered, the filtrate extracted with ether, the latter evaporated off, and the residue heated to 275° C. (to remove the last traces of ether and water). The commercial product thus obtained is purified by distillation. The reaction between the sodium *m*-benzenedisulphonate and sodium hydroxide may be represented as follows :—

$$C_6H_4(SO_3Na)_2 + 2\ NaHO = 2\ SO_3Na_2 + C_6H_4(OH)_2.$$

Sod. *m*-benzenedisulphonate — *m*-dihydroxybenzene.

Physical and Chemical Properties.—Colorless or faintly yellowish tabular or columnar crystals, with a scarcely perceptible urinous odor, and an unpleasant sweetish, pungent

taste; when pure and anhydrous it melts at 118° C. (100° to 111° C., Ph. G.) and boils at 276° C. It is readily and abundantly soluble in water (1:1 Ph. G.), alcohol (2:1 Ph. G.), and in ether, but scarcely at all so in cold benzene, chloroform and carbon bisulphide.

Heating to the melting point for a few miuutes with an equal weight of phtalic anhydride and added to water the "fluorescein" formed gives the latter an intense yellowish-green fluorescence. One grain warmed with 2 grains of tartaric acid and 10 drops of sulphuric acid forms a dark carmine-red liquid.

Inorganic impurities are detected by combustion on platinum foil; phenoloid bodies or acids by the odor and reaction with litmus paper—a feeble acidity should be allowed (Brenstein); and empyreumatic impurities by solution in ten times the weight in water (to which they communicate a yellow tint). Imperfectly refined products are detected by their low melting point; they can be purified by treatment with animal charcoal and crystallization.

Medicinal Uses.—Resorcin, as may be gathered from the formula, is allied to phenol, differing in the substitution of a hydroxyl group for a hydrogen atom. It also closely resembles that compound in its physiological and medicinal effects, but is free from the eminently toxic action of the monohydroxyl benzene. It was early recommended for its antiseptic and antipyretic properties (Andeer) against nausea and vomiting, gastritis (Menche, Andeer), and in asthma. The dose for internal use varies from 1 to 2 grains in seasickness, gastric affections, cholera infantum, etc., to 15 grs. against asthma.

Externally resorcin has been used in diphtheria, especially as a 10 per cent. resorcin glycerole for topical application, with injections of a 1 per cent. aqueous solution in the nasal form. A majority of observers obtained excellent results (Andeer, Callias, Cattani, Ehrhardt, Leblond, Baudier, and others), but a few voices have been raised against it (Nothnagel, Rossbach, Lœbisch, Lœffler). Locally used, a 1 per cent. solution being painted on the throat, very satisfactory results are recorded in whooping-cough (Moncorvo,

Bouchut, Callias, Mauriac, Andeer, Barlow, Guias). In ointment (5 to 10 or even 25 per cent.) resorcin has done good service in skin disease (Dreckmann), as also in the treatment of painful ulcers of the feet (Thoer). When solutions are used it is important to remember that weak solutions (1 to 3 per cent.) harden the skin, while stronger ones (10 to 50 per cent.) macerate and destroy it. Other forms in which resorcin has been used are in plaster-mull, wool, gauze (in general surgery), injection and sprays. A paste of equal parts resorcin and zinc oxide is employed to promote peeling of the skin in acne rosacea, applied to the affected part several times a day, and also for the removal of freckles and other superficial spots (Unna). The increasing employment for resorcin has led to its introduction into the U. S. Pharmacopœia.

DERIVATIVES AND ALLIED COMPOUNDS.

Resopyrin is the name of a compound of resorcin and antipyrine, obtained by the interaction of molecular proportions in solution (each in 3 parts of water); an abundant white precipitate is formed with some included oily drops. On violent agitation the oily mass increases and then suddenly solidifies to a hard, white, opaque body, resopyrin. From alcoholic solution it can be obtained in fine rhombic, odorless crystals, insoluble in water, but taken up by ether (1 : 100), by chloroform (1 : 30), and by alcohol (1 : 5); solution in the latter menstruum is not precipitated by water. It differs chemically from resorcin by not giving a precipitate with lead subacetate, nor a blue color with ferric chloride. When gradually heated it separates into two layers, an oily and an aqueous. The physiological and therapeutical action of this body are still undetermined.

Resorcylalgin is the name given to another compound of resorcin and antipyrine, obtained by interaction of the latter with resorcinate of potassium. It is described as sparingly soluble in water, easily soluble in alcohol, and possessing strongly acidic properties, in consequence of which it forms soluble salts with the alkalies, of which ammonium resorcylalginate is the chief; but no details of physiological or therapeutical valne are given.

Resorcinol is the name which has, in spite of being applied in England and in the United States to resorcin in accordance with modern chemical nomenclature, been also given to a brown amorphous substance, prepared from equal parts of resorcin and iodoform, and most likely only a partly decomposed mixture of the two substances. In the treatment of chancre, ulcers of the feet, gangrenous sores and various skin affections it has been employed successfully and is said to immediately alleviate itching (Bielajew). It may only be employed "pure" for gangrenous and atonic wounds, otherwise as a dusting powder mixed with four parts of starch, or as a 6 to 12 per cent. ointment with lard.

Acetonoresorcin is a compound of 2 parts resorcin with 1 part acetone, and occurs in small crystals, insoluble in water or alcohol, but soluble in alkalies. Therapeutical data are wanting.

Thioresorcin, $C_6H_4(OS)_2$, is a yellowish-grey, tasteless powder, insoluble in water, and only sparingly taken up by alcohol and ether. Has been used as an iodoform substitute for ulcers of the leg (Guttmann). Its application appears to be sometimes followed by unpleasant symptoms (Amon), though these may be traceable to admixture of resorcin.

Fluorescein, or resorcin-phtalein, $C_{20}H_{17}O_5$, occurs as dark-brown crystals, which form with ammonia a red solution, exhibiting a beautiful green fluorescence. Recommended for the diagnosis of corneal lesions, and detection of minute foreign bodies imbedded in that tissue. When an aqueous solution is dropped upon the cornea, those parts, however small, which are deprived of their epithelium are colored green, while foreign bodies are surrounded by a green ring (Straub). There seems to be some advantage in combining with the solution (10 grains to the ounce) one and a half times as much sodium bicarbonate (Randolph).

Hydroquinone, or paradihydroxybenzene, isomeric with resorcin, is prepared from aniline by oxidation with chromic acid mixture, and reduction of the quinone ($C_6H_4O_2$) formed by sulphurous acid. It is also a product of the splitting-up of arbutin by hydrolysis, thus:—

$$\underset{\text{Arbutin.}}{C_{12}H_{16}O_7} + H_2O = \underset{\text{Sugar.}}{C_6H_{12}O_6} + \underset{\text{Hydroquinone.}}{C_6H_6O_2}$$

Paradihydroxybenzene forms long, colorless, dimorphous crystals, melting at 169° C., difficultly soluble in cold water, readily so in hot water, in alcohol and in ether.

The compound has been employed as an antifermentative and antiseptic (Brieger, Lewin). In 1883 it acquired some reputation as an antipyretic (Silvestrini, Picchini, Traversa), the reduction of temperature taking place 30 to 40 minutes after the dose, 6 to 9 grains, Fresh solutions are free from caustic properties, and hence have been used subcutaneously and as injections in gonorrhœa (1 to 2 per cent. solution). The internal use of hodroquinone in typhoid has been suggested in doses of 3 to 8 grains.

As known, hydroquinone is largely used in photography as a developer.

Pyrocatechin, or orthodihydroxybenzene, the third of this group of isomers, with the general formula $C_6H_4(OH)_2$, occurs as acicular crystals, soluble in water, alcohol, ether and hot toluol; m. p. 104° C., b. p. 240° to 245° C. Aqueous solutions reduce silver salts in the cold, and Fehling's solution on warming; if made alkaline they absorb oxygen rapidly and change to green in color and finally to black. Pyrocatechin has been tried therapeutically as an antipyretic (Brieger, Masing), but abandoned on account of its by-effects.

SACCHARIN.

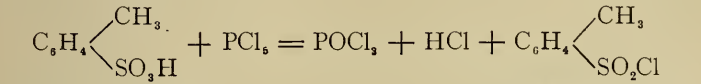
Synonyms: Benzoyl-sulphonic imide; Gluside; Glucusimide.

$$C_6H_4 \begin{Bmatrix} CO \\ SO_2 \end{Bmatrix} NH.$$

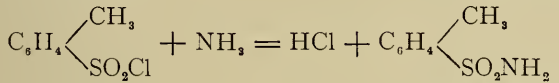
A derivative of the aromatic series, distinguished by its powerfully sweet taste.

Preparaton.—According to the patent specifications, by conversion of toluol into a sulphonic-acid compound, and of this into a sodium salt. By the action of phosphorus pentachloride the sodium salt is decomposed and a mixture of ortho and para toluol sulphochloride formed; the former isomeride is freed from the latter by cooling (when the para modification crystallizes out), and by the action of ammonia con-

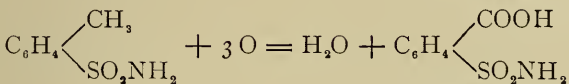
verted into orthotoluol-sulphamide. The next step is oxidation of the sulphamide into orthosulphaminbenzoic acid, which splits up into water and orthosulphaminbenzoic anhydride or benzoyl-sulphonic imide. The principle reactions are represented as under:—



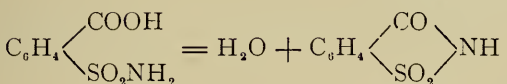
Toluolsulphonic acid. Toluolsulphochloride.



o.-Toluolsulphamide.



o.-Sulphaminbenzoic acid.



Saccharin.

By a new process of manufacture saccharin is prepared from *Thio-salicylic Acid* (*q. v.*).

Physical and Chemical Properties.—A white, uncertainly-crystalline powder, with an intensely sweet taste and a faint amygdaloid odor. Slightly soluble in cold water (1:400 at 15° C.), forming a feebly acid liquid; more soluble in alcohol (1:30) or glycerin; freely so in dilute ammonia, or in solution of sodium bicarbonate (evolving CO_2). According to the British Pharmacopœia Addendum, 1890, 100 parts of gluside mixed with water, warmed, neutralized with bicarbonate of soda, and evaporated to dryness, yield 113 parts of soluble gluside or saccharin. Probably in dissolving in water the acid is re-formed.

As evidence of identity the hepar reaction is officially adopted, and the absence of carbohydrates is ensured by providing that neither gluside nor soluble gluside shall be blackened when warmed with strong sulphuric acid.

Further proofs of purity are the absence of residue when heated on platinum foil, of a brown color when heated with

potash lye (grape sugar), and of a red precipitate when warmed with Fehling's solution (natural sugars). Salicylic or benzoic acids, if present, are detected by the violet color produced on addition of ferric chloride to the ethereal filtrate, mixed with ten times its volume of water. Mannite is detected by the azure blue color produced when a solution of soluble saccharin so contaminated is exactly precipitated by cupric sulphate, filtered, sodium lye added and boiled.

Commercial saccharin seems to be far from a pure or simple substance; it contains about 50 per cent. of impurities, consisting of the isomeric, and acid-tasting, para compound and of acid *o*-sulphobenzoate of potassium (Remsen and Burton, Dohome). The substance may be tested by treating with ether, which dissolves out the *o*- and *p*-benzoyl sulphonic imide and leaves undissolved all foreign matter. The para compound is estimated by digestion for several hours with 90 per cent. sulphuric acid, whereby *o*-benzoyl sulphonic imide is hydrolysed into *o*-sulphobenzoic acid and ammonium sulphate, whilst the para compound is unaltered and crystallizes out on cooling (Hefelmann).

For the detection and estimation of saccharin in food stuffs of all kinds, and especially in cane sugar, various processes have been suggested. According to Reischauer, 4 ounces of the suspected material (when this is cane sugar) are treated for a few hours with 6 to 10 oz. of ether, and filtered. If the sugar exhibit an alkaline reaction, instead of the solid substance, a concentrated aqueous solution feebly acidified with phosphoric acid should be shaken out with ether; in both cases the ether takes up the greater part of the saccharin contained in the sugar, which is left as a residue on evaporation and can be recognized by the taste, or in the following manner: The residue is melted gradually and carefully (otherwise violent explosion occurs) in a platinum capsule with a mixture of carbonate of soda and nitrate of potassium (6:1), and finally incinerated. The residue, dissolved in water, is tested for sulphates and the amount of sulphate of barium formed multiplied by 0.785 gives the weight of saccharin extracted; other compounds of sulphur possibly occurring in sugar are not taken up by the ether.

For the detection of saccharin in urine, C. Schmitt recommends that the liquid should be first tested for salicylic acid. If this be absent, 4 oz. of the strongly acidified liquid are shaken out three times with a mixture of equal parts of ether and petroleum ether, the extract mixed with soda solution and evaporated to dryness. The residue is heated for half-an-hour in a silver or porcelain capsule to 250° C., the mass dissolved in water acidified with sulphuric acid and shaken out with ether. The ethereal extract on evaporation of the solvent gives the ordinary reactions of salicylic acid (with ferric chloride for instance), produced in the decomposition of any saccharin present.

Beer is neutralized (about 2 pints being used) with sodium carbonate, evaporated to a syrupy consistence, and mixed by assiduous agitation with three or four times the volume of strong alcohol. After a few hours the mixture is filtered (the residue being washed with alcohol), the filtrate distilled, the residue taken up with water, diluted to about four or five ounces, strongly acidified with phosphoric acid, and shaken out three times with ether, each agitation being continued at least an hour. The ethereal solution is distilled, the residue neutralized with sodium bicarbonate solution, filtered and evaporated to dryness on a watch glass. The residue is recognized as saccharin either by the taste or by conversion into salicylic acid by heating with pure caustic soda to 250° to 270° C.

If salicylic acid be present in the beer, the ethereal residue, neutralized with soda, must be treated with mercuric nitrate, the precipitate (mercuric saccharinate) collected, washed, and dried by pressure between bibulous paper. It is then mixed, by melting, with excess of resorcin, a few drops of concentrated sulphuric acid are added, and the whole again warmed; the mass assumes various colors, froths and resinifies, while sulphur dioxide is given off. On cooling the mass dissolved in a little water gives with excess of caustic potash a deep brown liquid, with a green fluorescence, which is more pronounced if a few drops be removed and diluted with more water.

A great deal of discussion has centred around the question

whether saccharin is injurious to the animal organism or not, but it may be regarded as now established that it has no effect upon the system whatever. The compound passes through the body unchanged, and appears neither in the saliva nor in the milk but is entirely excreted by the urine. It seems to be without marked effect even upon the action of the animal ferments and upon micro-organisms in general, though the activity of *Saccharomyces cerivisiæ* was prejudiced by the presence of a quantity bearing the proportion to the yeast taken of 1:20 (Kornauth). Given in large doses continually to animals—which do not exhibit any disinclination to take the substance—saccharin had no appreciable effect upon the organism or upon the processes of nutrition.

Medicinal Uses.—The chief uses of saccharin in medicine are as a sweetening agent for the food of diabetics and as a general flavoring and corrective. For the former purpose its property of passing though the organism unchanged is believed to make it specially applicable. It has also been found to have a well-marked antiseptic action and has proved beneficial in the treatment of cystitis and urethral inflammation (Little, Colquhoun). By far the larger proportion seems to be used in sweetening various foods, confectionery, etc., and it seems to be generally unobjectionable for such purposes; as however, it is not a food it cannot substitute sugar in all cases, and hence the necessity for the many processes for its detection.

Ordinary saccharin containing the para-compound is generally stated at 300 times the sweetness of cane-sugar, but a refined saccharin, consisting solely of ortho-benzoyl-sulphonic imide, is produced of 500 times the sweetness of sugar. The soluble forms, prepared by admixture with carbonate of sodium or of potassium, have nine-tenths the sweetening power of the insoluble gluside.

An excellent and agreeable mouth wash is made by dissolving 10 grains each of saccharin and sodium bicarbonate in about 10 fluid drachms of spirit (warming gently to facilitate combination and the escape of carbon dioxide), adding 10 to 20 grains of salicylic acid, and making up to 1 fluid ounce with spirit. One teaspoonful of this spirituous solution

with 4 fluid ounces of water forms an effective solution for the purpose indicated.

For use in pharmacy various elixirs, syrups, etc., are prepared, and compounds of saccharin with certain bitter alkaloids and principles (*e. g.* quinine) have also been manufactured and employed in medicine.

DERIVATIVES AND ALLIED COMPOUNDS.

Dextro-saccharin is a mixture of 1 part saccharin with 2000 parts glucose.

Methyl-saccharin, $C_6H_3(CH_3):\begin{matrix}SO_2\\CO\end{matrix}>NH$, also prepared by a complicated process, is a bitter-tasting substance.

Chloro-, *Bromo-*, and *Iodo-saccharin* have also been prepared, and are of chief interest because of the well-marked gradation in their sweetening properties.

Dulcin, *Valzin* or *Sucrol*, $CO.NH_2.NH.C_6H_4.OC_2H_5$, are the names under which the paraphenetolcarbamide of Berlinerblau has been introduced as a sweetening agent. In constitution it is a substituted urea, para-ethoxyphenyl urea, and is prepared either by the action of potassium cyanate on para-phenetidine, or of carbonyl chloride and subsequent treatment with ammonia or urea. It occurs in colorless, crystalline needles, melting at 173° to 174° C., and dissolving in 25 parts alcohol, 150 parts boiling water, and 800 parts cold water. 1 grain dulcin heated in a test-tube to boiling with 5 drops concentrated sulphuric acid dissolves without coloration: on cooling, dilution with 4 drachms water, and pouring ammonia over the solution, a blue ring is formed at the point of contact between the two layers (Berlinerblau). Its sweetening power is about 200 times that of sugar. Earlier authors (Kossel) reported it to be comparatively free from physiological drawbacks and more agreeable to patients than other sweetening substitutes, but quite a number of authors, most recently Aldehoff, have found that with administration of 15 grains *pro die* to dogs, disturbances were visible from the very first, inducing vomiting, loss of appetite, apathy, and increasing emaciation, with the appearance of icterus and death in three weeks. Although the doses required for sweetening purposes

are comparatively small, great care should therefore be exercised in its exhibition.

Diabetin is chemically pure, crystallised *lævulose*, or fruit-sugar, $C_6H_{12}O_6$. Prepared from invert-sugar by precipitation as calcium salt, and decomposition of the latter with carbonic acid. A colorless and odorless crystalline powder, somewhat hygroscopic, and readily soluble in water and dilute alcohol. The aqueous solution reduces Fehling's solution, and rotates polarised light to the left (—25° for 5½ per cent. solution in 200 mm. tube). Diabetin is recommended as a carbohydrate sweetening agent for diabetic patients, because from recent investigations (Külz, Worms, Minkowski, Leyden and others) lævulose is much better economized in the diabetic system than dextrose, and by regular introduction of definite quantities of lævulose the sugar contents of the urine are not appreciably increased. The advantage of diabetin over the coal-tar sweetening agents is, that it is also a natural saccharine food that aids in the maintenance of the patient's strength.

SALACETOL.

Synonym: Salicyl-acetol.

$C_6H_4(OH)CO_2CH_2COCH_3$.

A salol compound in which the carbolic acid element is replaced by the acetone radicle.

Preparation.—Salacetol is prepared by heating together monochloracetone and sodium salicylate:

$C_6H_4(OH)_2Na + ClCH_2\ CO\ CH_3 = C_6H_4(OH)CO_2CH_2\ COCH_3 + NaCl$

Sodium salicylate — Monochloracetone — Salacetol

Physical and Chemical Properties.—Salacetol is a combination of salicylic acid in ester form with acetone alcohol or acetol, an absolutely non-toxic substance and the simplest homologue of lævulose or fruit-sugar. Salacetol may therefore be regarded as a synthetical glucoside.

It crystallizes in white shining leaflets, melting at 71° C.,

very slightly soluble in cold water, and scarcely in hot; in 15 parts of cold alcohol, and in 25 parts castor oil, or 30 parts of almond or olive oils it is completely soluble. It contains 71.1 per cent. salicylic acid, which is liberated by alkalies. As characteristic test the alkaline solution reduces Fehling's solution, and on acidification salicylic acid is precipitated (Helbing and Passmore).

Medicinal Uses.—Although of recent introduction Salacetol has proved clinically to be an excellent intestinal antiseptic in summer or choleraic diarrhœa, on account of its mild action and freedom from toxic-effects. It has also yielded excellent results in the treatment of rheumatism in its subacute and chronic forms, especially in conjunction with inunctions of salicylic acid lanolin ointment (Bourget). Administered in doses of 30 to 45 grains, dissolved in 1 ounce of castor oil, preferably before breakfast, in diarrhœa.

ALLIED COMPOUNDS.

Salicyl acetic acid, $C_6H_4(CO_2H)OCH_2COOH$, the product of the reaction between di-sodium salicylate and mono-chloracetate of sodium,

$$\underset{\text{Di-sodium salicylate}}{C_6H_4(ONa)CO_2Na} + \underset{\substack{\text{Mono chloracetate}\\ \text{of Sodium}}}{ClCH_2.COONa} = \underset{\text{Salicylacetate of Sodium}}{C_6H_4(OCH_2COONa)}\text{-}CO_2Na + NaCl$$

and liberation of the free acid from the sodium salt with hydrochloric acid, is said to possess great antiseptic properties. A salt of antipyrine prepared therewith is offered as a substitute for salipyrin, but no clinical reports have been forthcoming.

Saligenin, or *Salicylic-alcohol*, $C_6H_4(OH)CH_2OH$, the active component of the natural glucoside, salicin, has been up to the present excluded from therapeutical use by its difficulty of production. Recently, however, it has been easily synthesised by the condensation of phenol with formic aldehyde, according to the equation

$$\underset{\text{Phenol}}{C_6H_5OH} + \underset{\text{Formic aldehyde}}{H.CHO} = \underset{\text{Saligenin}}{C_6H_4(OH)CH_2OH}$$

and has therefore been introduced as a new salicylic preparation. Saligenin crystallizes in colorless leaflets, of slightly bitter taste, melting at 86° C., which are fairly soluble in cold, and easily in hot water and in alcohol.

SALICYLAMIDE.

$$C_6H_4\begin{cases}OH\\CONH_2\end{cases}$$

One of a large group of amidogen compounds, some members of which are well known in medicine (chloralamide, chloralurethane, urethane).

Preparation.—Preferably by the action of concentrated ammonia upon crude methyl salicylate as obtainable in the form of wintergreen oil. When these stand in contact (cold) for some days the liquid assumes a deep reddish-brown color and brownish crystals begin to separate; impurities are removed from these by recrystallisation and treatment with animal charcoal. It may also be obtained by the action of heat upon ammonium salicylate.

Physical and Chemical Properties.—When pure, salicylamide occurs in perfectly colorless, thin, transparent plates, melting at 142°C., soluble in alcohol, ether, chloroform and 250 parts of water (salicylic acid 1 : 500). It is quite tasteless, but produces a feeling of grittiness between the teeth. Salicylamide prevents the putrefaction of wine and other organic liquids for months.

Medicinal Uses.—This amide derivative of salicylic acid seems to closely resemble the parent substance in its therapeutical properties, but has the advantages of being tasteless and more soluble. It also acts more promptly, and in smaller doses is a more powerful analgesic and safer (Nesbitt). Salicylamide is excreted in the urine chiefly as salicyluric acid; as indicated above it has decided germicidal properties and retards diastatic and peptic change, though to a less extent than salicylic acid. In 3 to 5 grain doses (up to 15 grains a day) it was given successfully in ovarian pain, neuralgia, chronic rheumatism and follicular amygdalitis *(Ibid)*. In spite of its apparent advantages however, nothing further has been heard of it clinically.

SALOL.

Synonym : PHENYL SALICYLATE.

$$C_6H_4 \begin{cases} OH \\ COOC_6H_5. \end{cases}$$

One of the first synthetical organic salicylates, introduced into medicine in 1886.

Preparation.—Molecular proportions of salicylate of soda and sodium-phenol are caused to react by prolonged heating in the presence of phosphoric oxychloride. The reaction may be expressed as follows :—

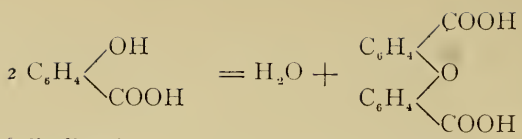
$$\underset{\text{Sodium phenol.}}{2\ C_6H_5ONa} + \underset{\text{Sodium salicylate.}}{2\ C_6H_4OHCOONa} + POCl_3 =$$

$$3\ NaCl + \underset{\text{Sod. phosphate.}}{NaPO_3} + \underset{\text{Salol}}{2\ C_6H_4OHCOOC_6H_5}.$$

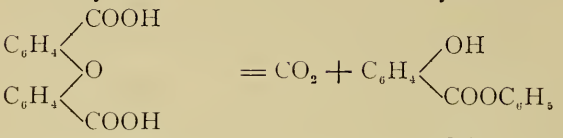
The product is treated with water, washed till practically free from chloride and phosphate, and finally crystallized from alcohol. It may also be obtained by leading phosgen gas into a warmed intimate mixture of salicylate of sodium and sodium-phenol. The reaction is quite similar to the above, except that the secondary products are sodium chloride and carbon dioxide.

A later patented process consisted in heating pure or even crude salicylic acid in a bath to 220° to 230°C. The vessel containing the acid has a narrow neck reaching so far out of the bath that at the temperature named the water vapors formed do not condense and fall back into the vessel but can be conducted away. If the neck be not heated much above the temperature necessary to ensure this only steam and carbon dioxide escape. Air is excluded by filling the vessel with an indifferent gas (*e. g.*, CO_2) and leading in a feeble stream of the same during the heating.

The most probable explanation of the reaction is that water is first split off, forming an anhydride-like body, and that this gives up carbon dioxide, and, intermolecularly, or with undecomposed salicylic acid, condenses to salol. For instance,



Salicylic acid. Anhydride.



Salol.

Physical and Chemical Properties.—A white crystalline powder, or transparant tabular crystals, with a faint aromatic odor, practically tasteless, being insoluble in water. It is taken up by 10 parts of alcohol, or less than its own weight of ether; an alcoholic solution forms with water a kind of emulsion. It is also considerably soluble in copaiba balsam, in sandalwood oil, in turpentine, and in fatty or mineral oils. Melting point 42° to 43°C.; heated on platinum foil it burns away without residue.

In a solution of ferric chloride an alcoholic solution of salol produces only a turbidity but no color; on the other hand, ferric chloride produces in an alcoholic solution of salol the characteristic violet color of phenol. Bromine water precipitates monobromsalol. The ether is split up by warming with the fixed alkalies into salicylate and alkali-phenol.

Free mineral acid (phosphoric) is detected by blue litmus paper. Free phenol or salicylic acid is evidenced by the behavior of an alcoholic solution with three times the volume of water, to which previously a drop or two of ferric chloride has been added; a permanent violet color is produced if these impurities be present.

Medicinal Uses.—Salol was prepared and introduced into medicine after physiological examination (Nencki, Sahli), as the result of researches with the view of discovering a compound of salicylic acid which should be free from the disadvantages of most salicylates. The first experiments showed that salol possessed antiseptic, antipyretic and antirheumatic properties, and it was especially recommended in rheumatism. At the same time it was found that the remedy being insoluble

passes unabsorbed and unchanged through the stomach and is only decomposed (into salicylic acid and phenol compounds) by the alkaline juices of the intestine. To this intestinal dissociation its particular virtues are largely due, as by its means local antisepsis becomes possible in such affections as acute diarrhœa, dysentery, cholera, etc. (Goelet, Cahall, Moncorvo, Nicholson, Löwenthal, Hüppe).

Being entirely excreted with the urine—which exhibits the characteristic dark color of phenol-urine—in the form of salicyluric acid and phenol compounds of marked antiseptic powers, salol has been administered internally in the treatment of affections of the bladder and urethra, *e. g.* catheter fever, fermentation of urine in the bladder, and especially gonorrhœa (Mumford, Lane, Griotzoff, Griwzow). For the latter purpose it may be combined with copaiba or sandalwood oil, in which it dissolves without difficulty. Good results are recorded from its use in gonorrhœal arthritis (Vernon Jones).

Some discussion has arisen as to the safety or otherwise of salol when given internally. Many authorities maintain that it may be given in large doses without risk (Georgi, Sahli, v. Jaksch), while others report symptoms of poisoning and even deaths after comparatively small doses (Hesselbach, Chlapowski). The remedy has, however, been very widely used without such untoward effects, and it seems likely that the cause of the toxic symptoms in the few cases alluded to should have been looked for elsewhere. It has been incorporated in the new edition of the U. S. Pharmacopœia.

The testimony on the value of salol in cholera epidemics is conflicting, and on the whole not satisfactory. Whilst at Warsaw, Russia, and in the Philipine Islands excellent results from its administration are reported (Walkovitch, Mitropolsky, Salvator), especially when given in large doses, in India it was abandoned after trial in 68 cases (Hehir), and in the Hamburg epidemic of 1892, it was also eventually considered useless (Reiche). There is some evidence that in the very violent disorder of the mechanism of digestion the remedy has no chance to act (Gironde).

As an intestinal antiseptic salol has, on the other hand,

an increasing reputation, especially in the treatment of typhoid fever (Posajnyi, Sympson, Lockwood, Anderson), and in infantile diarrhœa (Mensi).

Recent additions to the therapeutics of salol have also elucidated its value internally in pharyngeal inflammations (Gouguenheim, Caport), and combined with terpin hydrate (3 grains each) in bronchitis, catarrhal fever and colds generally (Cohen). It has also been tried in the treatment of leprosy and yellow fever. In diabetes mellitus the administration of salol has been attended with varying results, while in cases where an anti-diabetic regimen is impracticable or only partial it has a beneficial influence on the course of the disease, but it is contra-indicated in nephritis and albuminuria (Nicolaier).

The dose of salol as powder is 1 to 2 drachms daily in divided portions; in the diarrhœa and other intestinal troubles of children 2 to 3 grains may be given every three hours. In cholera, 8 grains salol has been prescribed in combination with 3 grains bismuth salicylate every three hours (Hüppe). In diabetes, doses of 30 grains three times daily have been attended with good results. Hypodermically salol has been used in solution of 1 part salol to 3 parts almond oil in the treatment of tuberculosis by Grossi.

Externally, the compound is used as an antiseptic and deodorant, similarly to iodoform, in the form of gauze, dusting powder (1 : 1 to 3 French chalk or starch), collodion (4 : 4 ether and 30 collodion), and of 5 to 10 per cent. alcoholic solution (with twenty volumes of water for gargling in angina, etc.). In ointments and compound powders it has been found the best remedy against impetigo, eczema, and sycosis (Saalfeld), and has also done good service as an insufflation in the treatment of ozæna.

A powder consisting of 15 grains salol, 3 grains salicylic acid, 2 grains tannic acid, and 1 grain powdered boric acid, has been recommended as an insufflation into each nostril for the aborting of acute coryza (Capitan). Some care appears, however, to be necessary in using it as it is not altogether free from caustic action upon the nasal mucous membrane if snuffed in too large quantities and too

frequently. The treatment should not be continued more than a few hours at most.

Spirituous solutions (about 5 per cent.) are employed with various flavoring agents for the preparation of mouth-washes and dentifrices, while it is largely used in the preparation of other toilet preparations, *e. g.*, powders and soaps.

Salol has also recently been recommended for coating pills intended only to develope their action in the duodenum, as only there is the coating dissolved and the ingredients liberated. Salol is simply melted and the pills dipped in, a coating of 1/3 to 1/2 grain being sufficient to secure impermeability, and of course it is advisable to have a thin coating in order to avoid the possibility of secondary symptoms arising from the introduction of carbolic acid into the system.

DERIVATIVES AND ALLIED COMPOTNDS.

Salol-camphor is made by mixing 3 parts of salol with 2 parts of powdered camphor, heating gradually to complete fusion, and filtering; the product is preserved in yellow hermetically sealed bottles. It is a colorless liquid of oleaginous character, insoluble in water, freely soluble in ether, chloroform and oils; under the influence of light and air it readily decomposed. Recommended in the treatment of purulent inflammation of the middle ear, pledgets of cotton-wool soaked in the camphorated salol being introduced into the external meatus previously thoroughly cleansed. Repeated every twelve or twenty-four hours, syringing with boric lotion in the intervals, this method cures most forms of suppurative otitis (Pégou).

Di-iodo-salol, $C_6H_2I_2(OH)CO_2C_6H_5$, the phenyl ester of diiodo-salicylic acid, is an odorless and tasteless powder, melting at 133° C., as yet not employed therapeutically.

Nitro-salol, $C_6H_4(OH)CO_2C_6H_4NO_2$, the salicylate of *p*-nitrophenol, obtained by condensation of the two constituents, is a yellowish-white, crystalline, insoluble powder, melting at 148° C., and split up by alkalies into its components. It is not itself employed therapeutically, but from it **Salophen** (*q. v.*) is prepared.

Methyl salicylate. $C_6H_4(OH)CO_2CH_3$, the essential constituent of the oil of wintergreen, has been introduced as a synthetical remedy into the U. S. Pharmacopoeia. Prepared by heating together salicylic acid and methyl alcohol in presence of dehydrating agents, as expressed by the formula:

$$C_6H_4(OH)COOH + CH_3OH = C_6H_4(OH)COOCH_3 + H_2O$$

Salicylic acid. Methyl alcohol. Methyl salicylate.

It is a colorless liquid, having the characteristic strongly aromatic odor, and the sweetish warm and aromatic taste of oil of wintergreen. Sp. gr. 1.185 at 15° C.: boils at 219 to 221° C., and is soluble in all proportions in alcohol, glacial acetic acid and carbon bisulphide. The alcoholic solution is neutral or only slightly acid to litmus paper. Like salol it is decomposed by alkalies, yielding a clear aqueous solution without any oily drops (absence of petroleum and other oily bodies), and on addition of a slight excess of mineral acid, salicylic acid crystallizes out. Methyl salicylate is employed as a substitute for oil of wintergreen.

For *Salacetol* and *Salicyl-acetic acid* see special article on **Salacetol.**

SALOPHEN.

Synonym: ACETYL-PARA-AMIDO-PHENYL SALICYLATE.

$$C_6H_4(OH)CO_2C_6H_4NHCOCH_3.$$

A salol compound in which the carbolic acid element is replaced by the acetylamidophenol group, which is the basis of phenacetine.

Preparation.—By the reduction and acetification of nitrosalol (*q. v.*), or by the heating together of salicylic acid and acetylparaamidophenol, $C_6H_4(OH)NH.COCH_3$, in the presence of phosphorus oxychloride. The final product is purified by recrystallisation from benzene or alcohol.

Physical and Chemical Properties. — Minute white crystalline scales, almost entirely insoluble in water, neutral in reaction, and free from odor and taste. Alcohol and ether take it up freely, and the alcoholic solution is colored violet by ferric chloride. Salophen melts at 187° to 188°C.,

and burns on platinum foil with smoky flame without leaving a residue. It dissolves readily in alkalies, being thereby split up into its components. On boiling the alkaline solution a blue color appears in the superficial layer exposed to the air, and on adding excess of hydrochloric acid, salicylic acid crystallises out, whilst the indophenol reaction (*vide* phenacetine) is given by the filtrate. The solution in concentrated sulphuric acid is colorless (absence of organic impurities), and the filtrate from 1 part salophen shaken with 10 parts water gives no precipitate with silver nitrate (chlorides) or with barium nitrate (sulphates). The crystals phosphoresce in the dark (Hitschmann).

Medicinal Uses.—Exhaustive pharmacological experiments with salophen showed that in the organism it is split up and excreted as salicyluric acid and acetyl-p-amidophenol compounds, and that it posesses very slight or no toxic action (Siebel), although sometimes a slowing of the pulse takes place (Hitschmann). It is further interesting to note that salophen has been observed to be excreted by the perspiration when taken internally, and small salophen crystals have even been obtained by evaporation of the sweat, whence it would appear that some enters the circulation undecomposed; but this is denied by other observers (Lütze).

According to most authors salophen is an excellent antineuralgic and an antirheumatic, but of no importance as an antipyretic (Köster), although in 20 cases of acute articular rheumatism its antipyretic effect was very marked (Froehlich). It appears to be specially indicated in acute forms of rheumatism (Guttmann, Hitschmann, Hare, Koch, Gerhardt, Lütze, Osswald, Hardenbergh), and is less disturbing than salicylate of soda and other remedies, but in chronic rheumatism it is comparatively useless. Most useful has salophen been found in cephalalgias, neuralgias and migraine, all the above authors as well as others regarding its action as satisfactory in nervous affections of various forms. Administered in doses of 15 to 30 grains once or twice daily in neuralgic affections, and in doses of 1 to 1½ drachms in acute rheumatism.

SOZOIODOL.

Synonym : Di-iod-para-phenol-sulphonic Acid.

$C_6H_2I_2OHSO_3H + 3\ H_2O$.

A crystalline monobasic acid, introduced in 1887 as an antiseptic; it contains 52.8 per cent. of iodine and 7 per cent. of sulphur.

Preparation.—By the interaction of potassium paraphenolsulphonate, dissolved in dilute hydrochloric acid, and a solution of potassium iodate and iodide, in molecular proportions (or of iodine chloride). Finely-divided iodine first separates, and then again re-dissolves. After a short time long white needles come out of solution, which are the potassium salt of sozoiodol.

Physical and Chemical Properties.—Sozoiodol crystallizes from water in acicular prisms, which lose their three molecules of water of crystallization when exposed over sulphuric acid. It is readily soluble in water, in alcohol and in glycerin. The aqueous solution has an acid reaction and gives a violet-blue coloration with ferric chloride. The addition of nitric acid causes a separation of iodine.

The presence of iodide or of chloride is detected by the precipitate formed when argentic nitrate is added to a solution of sozoiodol in nitric acid, and of sulphate by the insoluble precipitate formed on the addition of barium chloride. (Barium sozoiodol is soluble in boiling water).

Medicinal Uses.—Sozoiodol was put forward as combining in itself the antiseptic and general therapeutical virtues of iodine and carbolic acid; at the same time it could not manifest the poisonous properties of the latter as the phenol was present in the form of the harmless compound carbolsulphonic acid. In the organism it does not appear to be split up but is resolved into and excreted as an organic compound of uncertain nature, which has no irritating influence upon the kidneys (Langgaard and Buffalini).

In 2 per cent. solution both sozoiodol and sozoiodol sodium entirely prevent the development of pus cocci. Its absolute freedom from odor, its solubility and stability under normal conditions constituted its chief claims of preference

over other iodine compounds. It has been used in all cases where iodoform is considered indicated.

Either the acid itself, or its preparations, has been employed in skin diseases (Lassar, Schwimmer, J. Koch), in rhinopharyngology (Fritsche, Seifert, Herzog, Stern), in gynæcology (Nitschmann), and in general surgery, burns, etc. (Thomann, Ostermayer). In venereal diseases, gastric affections, and rheumatism its successful use has been also reported, while further it has been recommended in dental surgery and in veterinary practice.

The forms in which the compound is applied resemble those adopted generally for iodoform and its substitutes, *e. g.* dusting powder (5—10—20 per cent. with French chalk) collodion, solutions, gauze, etc.

DERIVATIVES AND ALLIED COMPOUNDS.

The salts of iodophenolsulphonic acid, or at least the most important described below, have been more employed than the parent substance.

Potassium and *sodium sozoiodol*, $C_6H_2I_2(OH)SO_3K$ (or Na) + 2 H_2O, form colorless, well defined prisms, soluble in water —the potassium compound in 50, the sodium in 14 parts. The solutions are acid, and give a bluish violet with ferric chloride. Fuming nitric acid displaces iodine, picric acid being simultaneously formed; barium chloride produces a precipitate, soluble on boiling. The aqueous solutions gradually darken under the influence of light. Preferable to iodoform in the treatment of ulcers (Rosinski).

The sodium salt has yielded better results in idiopathic ulcerative processes than in those of syphilis. In vesical affections the bladder is irrigated with a 1 per cent. solution, and the same application is recommended in catarrhal conditions of the nasal mucous membrane. Also employed freely in pertussis in insufflations of 3 grains into each nostril once a day (Guttmann).

Zinc sozoiodol crystallizes in colorless needles with six molecules of water; it is soluble in water (1 : 20) and in alcohol. In ½ per cent. solution this salt has done good service in acute and chronic blennorrhœas and in a few cases of catarrhal inflammations of the nasal and pharyngeal

mucous membranes, either as a powder with 10 to 15 parts of French chalk, as paint or mouth wash.

Mercury sozoiodol, $[C_6H_2I_2(OH)SO_3]_2Hg$, is a lemon-yellow subtile powder, scarcely soluble in water (1 : 500), but much more readily in sodium chloride. In 10 per cent. solution it appears to have a strongly irritant action. "With respect to its curative value this preparation is superior in certainty of effect to all other sozoiodol preparations" (Schwimmer). It has been chiefly used in the specific treatment of syphilis, locally and subcutaneously, as combining the freedom from local effects of soluble mercurials with the prolonged and energetic action of the insoluble. Dose, 1 grain in the gluteal region. Also employed to remove polypi from the ear (Klamann) and as a 1 per cent. ointment or dusting powder for perspiring feet (Witthauer).

Picrol, or the potassium salt of *di-iodo-resorcin-monosulphonic acid*, $C_6HI_2(OH)_2SO_3H$, the complete analogue of sozoiodol, has been preparedby Darzens and Dubois, and acquired the name from its bitter taste. It is a pure, colorless and odorless, crystalline powder, of acid reaction, soluble in alcohol, ether and in collodion, and in water in the proportions of 1 to 5. Picrol contains 52.8 per. cent. iodine, and is put forward as a strong but non-poisonous iodoform substitute.

Di-iodo-salicylic acid, or *di-iodo-phenolcarboxylic acid*, $C_6H_2I_2(OH)COOH$, prepared by the action of iodine and iodic acid on salicylic acid in alcoholic solution, has been recommended in the form of its sodium salt for employment in parasitic skin diseases. The acid and its salt also possess analgesic and antipyretic properties, and have been given in doses of 25 to 60 grains pro die in rheumatism, instead of salicylic acid, but appear to interfere with the heart's action.

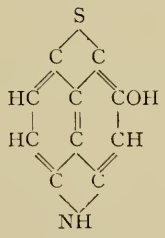
Losophan, or *Tri-iodo-meta-cresol*, $C_6HI_3(OH)CH_3$, prepared by the direct action of iodine on meta-cresol, or better on *o*-oxytoluic acid, in the presence of a definite quantity of alkaline carbonate sufficient to neutralize two-thirds of the hydriodic acid formed.

$$\underset{\text{o-oxytoluic acid}}{C_6H_3(OH)(CH_3)CO_2H} + Na_2CO_3 + 3I_2 = \underset{\text{Tri-iodo-meta-cresol}}{C_6HI_3(OH)CH_3} + 2NaI + HI + H_2O + 2CO_2$$

With more alkali iodine derivatives of the aristol type (*q. v.*) are formed. Losophan occurs in colorless, odorless crystals, of slightly acid reaction, melting at 121.5° C. It is practically insoluble in water, so that its watery solution is not colored blue or violet by ferric chloride (free phenols). It dissolves slowly in alcohol, easily in ether, chloroform and fatty oils. Dissolved also without change in dilute alkalies, but converted into a greenish-black amorphous substance, insoluble in alcohol, by concentrated caustic soda solution. Losophan, which contains 78.4 per cent. iodine, was recommended as of considerable value in animal and vegetable parasitic affections of the skin by Saalfield, who employed it in 1 or 2 per cent. alcoholic solutions or in 1 to 10 per. cent. lanolin or vaseline ointments, but no further clinical reports have been published. It is contraindicated in inflammatory conditions.

SULPHAMINOL.

Synonym: Thioxydiphenylamine.



Preparation.—By the action of sulphur "in a suitable manner" upon the salts of *m*-oxydiphenylamine dissolved in water.

Physical and Chemical Properties.—Sulphaminol is a pale-yellow powder, free from odor and from taste; readily soluble in alkalies, more difficultly so in alkaline carbonates, quite insoluble in water. It is taken up by alcohol as well as by glacial acetic acid; the solutions are colored pale yellow. When subjected to the action of heat it turns brown, and melts at about 155° C.

Medicinal Uses.—Pharmacological investigations have shown that thioxydiphenylamine is perfectly harmless, both

to animals and to human beings (Kobert, Wojtaszek); when taken internally it is split up in the organism into oxydiphenylamine and sulphuric acid compounds. Sulphaminol possesses marked antiseptic properties which render it suitable for application to the same purposes as iodoform. It has been successfully employed in pharyngeal tuberculosis, and further for the so-called dry treatment of suppurative processes of the jaw. The offensive odor of the latter is only to be overcome by the application of iodoform or of sulphaminol (Moritz Schmidt). In the form of dusting powder it produces strikingly rapid and favorable results in rhinolaryngology (Robertson), in wounds, ulcers of the feet and bed-sores; has also proved beneficial internally against cystitis (Rabow). The single dose amounts to 4 grains in powder, the daily dose to 15 grains. In another case of cystitis and soft venereal ulcer no appreciable effects were produced by the employment of sulphaminol (Wojtaszek). It has been specially recommended for curing the so-called "putrid-brood" of bees, being several times applied in powder.

DERIVATIVES AND ALLIED COMPOUNDS.

Under the names *Sulphaminol-menthol, S.-creosote, S.-guaiacol, S.-eucalyptol,* solutions of the compound in the different liquids named have been introduced into commerce, and brought under the notice of the medical world, especially for use in rhino laryngology and laryngeal tuberculosis.

Thiuret, $C_8H_7N_3S_2$, is a sulphurated base obtained by the action of weak oxidizing agents on phenyldithiobiuret. The latter is treated in warm alcoholic solution with iodine as long as it absorbs it, and the excess of iodine is removed, whereupon the hydriodide of thiuret crystallises out with one molecule of alcohol. This is dissolved in boiling water, and dilute ammonia added to the cooled solution. The free base thiuret is precipitated as a voluminous crystalline powder. The principal salt is

Thiuret phenolsulphonate, $C_8H_7N_3S_2.C_6H_4(OH)SO_3H$, a yellowish-white, odorless, crystalline powder, of intensely bitter taste. It melts at 215° C, and dissolves in 350 parts water at 15° C. In alcohol, ether and oils it is insoluble. The aqueous

solution gives a violet coloration with ferric chloride, and a voluminous white precipitate of thiuret base with dilute ammonia. In boiling alkalies thiuret dissolves, and on acidification phenyldithiobiuret is precipitated and sulphuretted hydrogen evolved. Boiled with acids both sulphuretted hydrogen is evolved and sulphur precipitated. Thiuret possesses in a very marked degree kolyseptic and germicidal powers, and is recommended as a substitute for iodoform (Blum).

The *hydrochloride, hydrobromide, salicylate* and *cresotinate* of *thiuret* have also been prepared.

Thiophene, C_4H_4S.—This body, closely allied to pyrrol and furfuran in constitutron, was discovered in coal tar benzene by Victor Meyer in 1883. It forms a colorless, mobile, oily liquid, with a feeble odor, boiling at 84° C., and not miscible with water.

The compound itself has not been employed in medicine, but two derivatives have,—namely, sodium thiophenesulphonate (C_4H_3S-Na SO_3) and thiophene diiodide ($C_4H_2I_2S$). The former is a white crystalline powder, and contains 33 per cent. of sulphur. The diiodide crystallizes in beautiful tables; it is insoluble in water, but taken up abundantly by the other usual solvents. Thiophene diiodide melts at 40.5°C., and is volatile at ordinary temperatures: it contains 9.5 per cent. of sulphur.

The sodium salt was used with good success in prurigo (Spiegler), proving superior to β-naphtol, non-poisonous and non-irritating; it can be used where β-naphtol is contra-indicated.

The diiodide was employed externally as gauze and as powder in a number of cases where iodoform is the usual application, such as mammary carcinoma, phlegmonata, mastitis, caries, bursitis, and certain surgical cases. Symptoms of poisoning were never observed, nor did eczema form. On the other hand, secretion dried up, deodoration was perfect, and granulations firmer than those which developed under iodoform (Hock, Zuckerhandl).

Thiosinamine, Allyl-sulpho-urea, or *Rhodallin,* $CS(NH_2)NH$-C_3H_5, is prepared by warming together 3 parts mustard oil,

3 parts alcohol and 6 parts ammonia, at 50° C. The mustard oil odor disappears, the originally turbid solution clears, and deposits crystals of thiosinamine on cooling, which are recrystallised from 2 parts boiling water.

$$CSNC_3H_5 + NH_3 = CS(NH_2)NHC_3H_5$$

Allylsulphocyanide — Allylsulphourea

The crystals are colorless or slightly yellow, with an alliaceous odor, melt at 74° C., and are easily soluble in water alcohol and ether. Employed with benefit in the treatment of lupus in the form of a hypodermic injection of a 15 to 20 per cent. alcoholic solution. Cicatricial tissue was softened, glandular swellings diminished and exudations absorbed without any general systemic disturbance (Hebra). It also possessed peculiar beneficial action on cicatricial tissue in tumors of the uterine appendages, slight perimetritis and salpingitis (Latzko) but of transient duration only (Hanc). On account of its reducing properties, thiosinamine has also been introduced into photographic practice as a substitute for "pyro".

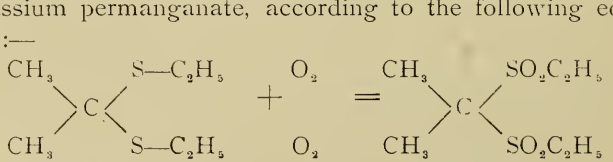
SULPHONAL.

Synonym : Di-ethyl-sulphon-dimethyl-methane.

$$(CH_3)_2\,C\,(SO_2C_2H_5)_2.$$

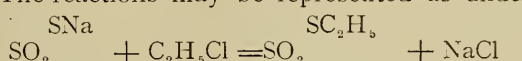
A synthetic hypnotic which has been admitted into the official materia medica of several countries.

Preparation.—By the interaction of anhydrous mercaptan, and anhydrous acetone in the presence of a stream of dry hydrochloric acid gas. The liquid gradually becomes turbid and separates into two layers, of which the upper is mercaptol (dithioethyldimethylmethane, $[CH_3]_2C[SC_2H_5]_2$), the lower dilute hydrochloric acid (the water is a product of the reaction). The mercaptol is separated, washed, and oxidized by potassium permanganate, according to the following equation :—

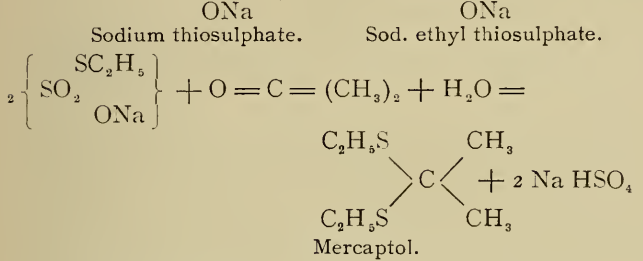


Mercaptol. Sulphonal.

It is also manufactured by the action of ethyl chloride or bromide on sodium thiosulphate, conversion of the resultant sodium ethyl thiosulphate into ethyl mercaptan and acid sulphate of sodium by the action of water. As this conversion takes place in the presence of alcoholic hydrochloric acid solution and acetone, the ethyl mercaptan is condensed *in statu nascendi* to mercaptol, which is oxidized as above described. The reactions may be represented as under:—



Sodium thiosulphate. Sod. ethyl thiosulphate.



Mercaptol.

The third stage is the oxidation of mercaptol to sulphonal, already illustrated.

Physical and Chemical Properties.—Colorless, inodorous, practically tasteless, prismatic crystals, melting at 125° to 126° C. (B. P. Add. 125.5° C.). Soluble in 15 parts of boiling water, and in about 450 parts of that solvent cold; also in cold rectified spirit (B. P. Add. in about 50 fluid parts), and freely in boiling alcohol; soluble in ether (1:135 at 15°).

Sulphonal is a very stable body, being unaffected by concentrated acids, alkalies, or oxidizing agents, either in the cold or when warm. Chlorine and bromine also are without effect even when warmed. To this stability must be ascribed the lack of a characteristic reaction for the compound.

Officially, sulphonal must burn away without residue when ignited with free access of air. The test of Vulpius, according to which the repulsive odor of mercaptan is evolved when sulphonal is heated with potassium cyanide, is recognized in the Pharmacopœia, and it is added further, that "when to the solution of the product in water excess of

hydrochloric acid and a few drops of solution of perchloride of iron are added a reddish color is developed." This color is due to the formation of ferric thiocyanide. The same effect may be produced by heating sulphonal with gallic or pyrogallic acid, or with wood charcoal. The reaction is not peculiar to sulphonal, but it is produced by the whole classes of sulphones and disulphones, and by most mercaptan derivatives.

Further tests of the purity of the compound are that the solutions must be neutral and unaffected by barium or silver nitrates. Two ounces of a hot 2 per cent. solution must not immediately decolorize 6 drops of volumetric potassium permanganate solution.

The urine of patients who are taking considerable doses of sulphonal assumes a peculiar reddish-brown color, due to the presence of hæmatoporphyrin. This substance is best detected by observing the spectroscopic behavior of the solution in hydrochloric acid and ammoniacal solution; or the color may be precipitated by alkaline barium chloride solution, and the solutions obtained by treatment of the precipitate with alcohol containing hydrochloric acid spectroscopically examined (Salkowski). The appearance of hæmatoporphyrin in the urine is one of the first indications of an incipient toxic action of sulphonal, and therefore attention should always be paid to the color of the urine of patients to whom sulphonal is administered (Schaeffer).

Medicinal Uses.—Sulphonal was introduced in 1888 as a hpynotic, which induced quiet and sound sleep, from which the patient awakened refreshed and free from any after-effects; blood pressure was not affected nor the blood itself, nor the digestive tract (Kast, Rabbas, Salgo, Rosin), and it was given by a long list of observers in mental diseases, in trismus, in nervous sleeplessness, and insomnia from pain and cough, etc. (Cramer, Oestreicher, Schwalbe, Fraenkel, Ott, Matthes, Ruscheweyn, Kronfeld, Löwenthal, Conolly, Norman, Mahon, Berenyi and many others). It was not long, however, before cases of unpleasant after-effects, poisoning symptoms, and even fatal issues after the administration of sulphonal began to multiply. Indictments against

the remedy were brought by a number of observers (Schotten, Joachim, Garnier, Knoblauch, Vorster, Knaggs, Montzel), some of which characterized it as less a remedy than a poison! Opinions and experience are, however, far from unanimous on the point.

In spite of disappointing results and toxic effects in some cases, the advantages of the drug when used with care, and under medical supervision, are too evident to allow it to be discarded. As the toxic effects arise from cumulative action, it is suggested that its administration be interrupted from time to time so as to secure elimination,—anorexia, vomiting or pains in the stomach, as well as the coloration of the urine, being regarded as indications for immediate discontinuance (Kast, Goldstein). Purging the alimentary canal from time to time is also recommended, for just as long as it is kept free and the kidneys act efficiently and normally, the drug may be considered harmless (Fuerst).

Two propositions have been made which are claimed to increase the value of sulphonal as a hypnotic. One is to combine each dose (15 grains) with ½ to 1 grain of codeine (Svetlin) or of morphine (Gonzales), and the other is to dissolve the remedy in boiling water, add carefully just sufficient cold water to make the draught potable (or allow to cool sufficiently) and take immediately before bed-time. The action is more prompt, the sleep sounder, and after-effects (drowsiness, etc.) more rare (Stewart).

The dose of sulphonal is from 15 to 40 grains, and it may be taken in powder (wafers), substance, or in solution as described in the preceding paragraph. In 8 grain doses it has been prescribed against the night sweats of consumptives.

DERIVATIVES AND ALLIED COMPOUNDS.

Trional, $C_2H_5CH_3 . C . (SO_2C_2H_5)_2$, differs from sulphonal (as can be seen by comparing the formulas) only in the substitution of an ethyl for a methyl group, so that its systematic name is diethylsulphonmethylethylmethane. It forms lustrous, tabular, bitter crystals, melting at 76° C., requiring 320 parts of cold water for solution, but readily soluble in alcohol and in ether. This compound was expected to be a more power-

ful hypnotic than sulphonal, from the physiological experiments performed on animals (Baumann and Kast). Barth and Rumpel found that though evidently indicated in certain nervous diseases where sulphonal did not answer, the dose had to be quite as large. It seemed, however, to be less liable to produce ill-effects than sulphonal, and this opinion has been gradually strengthened with increasing knowledge and employment of the drug.

In a very important series of physiological experiments carried out recently in Baumann's laboratory as to the fate of trional and its two homologues, sulphonal and tetronal, in the human system, it was found that trional alone did not appear in the urine after continued administration daily, being completely decomposed and absorbed in the system, wheras sulphonal and, to a large extent, tetronal were eliminated unaltered in the urine in daily increasing quantities. Trional is therefore free from the delayed cumulative action of sulphonal, because it is more easily and completely decomposed in the system (Morro). In these experiments the respective sulphones were isolated from the urine by repeated extraction with alcoholic ether, treatment of the residue with caustic soda, and re-extraction with pure ether, from which on evaporation the sulphone was obtained in a pure crystalline state. Control experiments show the method to be very exact.

Clinical reports of the employment of trional confirm the deductions of physiological experiments and are rapidly accumulating, showing trional to be a good and safe hypnotic, comparatively free from drawbacks, and apparently destined to become the most important drug of the sulphonal group. The dose generally adopted is 30 grains. In simple insomnia a dose of 15 to 30 grains is sufficient to produce sleep in 15 minutes and even in conditions of psychical excitement, it is most useful with a maximum dose of 45 grains (Boettger). In insanity it has been found very successful without any dangerous ill-effects (Collatz, Schaeffer). In 32 cases of mental disorder trional was found to be a good hypnotic and in many cases a sedative, being specially successful in maniacal attacks and in alcoholic pseudo-paralysis and psy-

chosis, but uncertain or of little avail in hysteria, paralysis, or epilepsy (Pelanda and Rainer). It is said to have a specific and certain action in all cases of agrypnia, and to be most valuable in psychiatric treatment (Grünfeld); it has been employed in a large number of cases of agrypnia arising from morphine, cocaine and chloral habits with the best results.

Quite a number of other authors testify to the safe hypnotic action of the drug (Schultze, Horvath, Raimondi and Mariottini, Schaefer, Boettiger, Brie, Bakofen, Hammerschlag). If not given in too large doses, the patient wakes bright and cheerful (Beyer). The drug is superior to sulphonal because it acts more rapidly and procures calm sleep and a normal waking (Vogt). Toxic urinary symptoms have been seldom observed (Schultze) or not at all (Bakofen). According to Vogt the hæmatoporphyrinuria, which is a sign of incipient toxic action as with sulphonal, is only manifested when the urine is strongly acid in reaction, and it is therefore well to administer alkalies with the drug.

Tetronal, $(C_2H_5)_2 . C . (SO_2C_2H_5)_2$, or diethylsulphondiethylmethane, occurs in lustrous tabular crystals and plates, which melt at 85° C. It is soluble in 450 parts of cold water, readily so in alcohol, and fairly in ether. The taste is camphoraceous and bitter. The name, of course, like "trional," which it physiologically and therapeutically resembles, has reference to the number of ethyl groups present. Early physiological experiments on animals indicated that tetronal had even a more pronounced hypnotic action than trional (Baumann and Kast), but recent experience has shown that although a few authors (Horvath, Schaeffer) give tetronal the preference, generally trional is more active than tetronal and altogether has been found more useful. The recent experiments in Baumann's laboratory (*v.* trional) have shown that tetronal behaves more like sulphonal in the system, being less easily absorbed than trional, and hence exhibiting a delayed cumulative action which is productive of the bye-effects observed in its use (Morro). With reference to the comparative stability of sulphonal and tetronal in the system, it is interesting to observe that both of these compounds have sym-

metrical chemical formulae, whilst trional is an asymmetrical compound.

SYMPHOROL.

Synonyms: Caffeine sulphonate; Nasrol.

A caffeine derivative prepared in accordance with the observation of Heinz and Liebrecht that on the introduction of the sulphonic acid group into the molecule of substances having an action on the nervous system, the latter is thereby annulled without, as a rule, further interference with its physiological properties.

Physical and Chemical Properties.—Symphorol is presented in the forms of the sodium, lithium and strontium salts of caffeine-sulphonic acid, which are distinguished by the suffixes *Symphorol N* (= natrium), *Symphorol L* and *Symphorol S*, respectively. They are all white, micro-crystalline powders, devoid of odor, of bitter taste, and soluble in water. The sodium salt is least soluble, dissolving slowly in 50 parts cold water, readily in 6 or 8 parts boiling water; but as crystallization only takes place very slowly from supersaturated solutions, ten per cent. solutions do not deposit for several hours, and five per cent. solutions may be kept several days without signs of crystallization. Insoluble in alcohol, ether and chloroform.

On evaporation with chlorine water and treatment of the residue with ammonia the well-kown purple coloration or murexide reaction of caffeine is given by the salts of caffeine-sulphonic acid. They are readily distinguished from the alkaloid caffeine, however, by (1) insolubility in chloroform. (2) non-precipitation from aqueous solution by tannic acid. (3) emission of sulphuretted vapors of peculiar odor on ignition, and (4) production of considerable ash on incineration (Helbing and Passmore). The sodium, strontium and lithium salts are most readily distinguished amongst themselves by their flame reaction.

Medical Uses.—Symphorol possesses a most pronounced diuretic effect in consequence of the irritating action of caffeine on the nerve-centres, and its contractile effect on the vascular system, being overcome, whilst the "somatic" or stimulant action of caffeine on the renal secretory cells is fully developed (Heinz & Liebrecht). Numerous blood-pressure experiments have demonstrated that neither large nor small doses increase the blood-pressure in the slightest degree, nor is there the slightest deleterious effect on the heart visible.

With administration of 60 grains symphorol in the course of the day, the elimination of urine during the next 24 hours is very greatly increased, being doubled in healthy persons. No disturbing effect on the stomach or intestines is experienced; the appetite is not affected nor the peristaltic movements interfered with. On account of the safe and reliable diuretic action of symphorol it appears destined to play an important role in the future treatment of dropsical affections and all disorders where increased diuresis is beneficial.

The sodium salt or Symphorol N is usually employed. The lithium salt (Symphorol L) is specially indicated in gout and uric acid diathesis, where the remedial action of lithium will be favorably influenced by combination with an acid of diuretic action assisting more rapid elimination of uric acid. The strontium salt (Symphorol S) is recommended for use in renal inflammation, where, according to recent French investigators, strontium salts (*vide* Appendix) are most beneficial.

Symphorol may be administered in doses of 15 grains four times a day, either dissolved in water, or, if the bitter taste be objected to, in capsules.

TANNIGEN.

Synonym: Diacetyl-tannin.

An acetic acid ester of tannin, prepared by the moderated action of glacial acetic acid and acetic anhydride on tannin.

Physical and Medical Properties.—A yellowish-grey, slightly hygroscopic powder, both tasteless and odorless.

Browns and commences to melt at 187° C., when dry. It is insoluble in cold water and dilute acids, and only soluble to a very slight extent in ether or hot water. Easily soluble in cold alcohol or in dilute solutions of phosphates of potassium or sodium, borax, lime, etc.

Tannigen is saponified in a short time by boiling soda or potash solutions, or gradually in the cold, into acetic and gallic acids. Ammonia produces tannic acid. Ferric salts produce the characteristic blue-violet reaction of tannin in its solutions. A slightly alkaline solution in phosphate of sodium precipitates gelatine and albumen and exhibits all the characteristics of an astringent. The addition of alkali or borax annuls the precipitant and astringent properties.

Medicinal Uses.—As a consequence of the insolubility of Tannigen in water and dilute acids and its saponification by alkaline liquids, it has been recently recommended as an intestinal astringent which passes the stomach unaltered and only develops its action amongst the alkaline intestinal juices. Taken by animals in comparatively large quantities without any disturbance of the appetite or digestion (Hans Meyer). Clinical experience limited. Especially successful in chronic diarrhœa of various origin, decreasing the number of stools and increasing their consistency on the second day, in doses of 3 to 8 grains three times a day (Müller). Large doses can be taken without evil effects. In acute diarrhœa results, so far, less decisive. Also insufflated into the nose in chronic inflammatory conditions of nose aud larynx, and employed as a gargle in chronic pharyngitis in the form of a 3 per cent. phosphate of sodium solution.

ALLIED COMPOUND.

Tannin Albuminate has also been recommended as preferable to ordinary powdered tannin, in that it has a more agreeable taste and is rapidly absorbed from the stomach without causing any disturbance. At the same time its astringent action is as marked, or even more so, than that of Tannin.

THALLINE.

Synonym: Tetrahydroparachinanisol.

$C_9H_{10}N(OCH_3)$.

A liquid base, first prepared in 1885 by Skraup, who also effected the synthesis of chinoline.

Preparation.—According to the patent specifications, from parachinanisol, obtained by heating together para-amidoanisol and acrolein (= glycerin + sulphuric acid) in the presence of an oxidizing agent (paranitroanisol). By reducing agents parachinanisol takes up four hydrogen atoms, forming the base thalline. These two reactions may be represented as follows:—

$$\underset{\text{Para-amidoanisol.}}{C_6H_4NH_2CH_3} + O + \underset{\text{Acrolein.}}{CH_2CHCHO} = \underset{\text{Parachinanisol.}}{C_9H_6N(OCH_3)} + 2\ H_2O.$$

$$C_9H_6N(OCH_3) + 4\ H = \underset{\text{Tetrahydroparachinanisol.}}{C_9H_{10}N(OCH_3)}.$$

Physical and Chemical Properties.—At ordinary temperatures thalline is an oily liquid, solidifying when cooled to yellowish crystals. It has a strong odor, resembling cumarin, and forms well defined salts with acids.

Oxidizing agents (the halogens, the nitrates of silver and mercury, chromic acid, ferric chloride, etc.) produce an intense emerald green color, hence the name (*θάλλος* a green twig. — Ferric chloride produces the color (which is not affected by addition of a drop or two of pure concentrated sulphuric acid) in very dilute solution (1:100000). Sodium thiosulphate changes the green tint into violet and then into wine-red, oxalic acid at ordinary temperatures into pale yellow, deepening into saffron on heating.

Medicinal Uses.—The base thalline itself is not suitable for use in medicine, and of the possible salts only the sulphate and tartrate have been used.

Thalline sulphate is a yellowish-white, crystalline powder, with a cumarin-like odor, and a taste described as at once acid, saline, bitter and spicy. Soluble in seven parts of cold or 0.5 part of boiling water; also in alcohol (1:100), difficultly so in chloroform, and practically insoluble in ether. The aqueous solutions are acid, and when exposed to light gradu-

ally darken; by iodine solution they are precipitated brown, by tannic acid white, and by Nessler's reagent lemon-yellow. Like the base itself this salt in 1 per cent. solution is colored emerald green by ferric chloride. When heated over 100° C. thalline sulphate melts, and if the temperature be raised it decomposes, burning away (if pure) without residue.

Thalline tartrate occurs as a yellowish-white, crystalline powder, with an odor reminding of anise and cumarin; soluble in water (1:10), slightly so in alcohol, and practically insoluble in ether and in chloroform. In general it behaves like the sulphate, but is distinguished by giving no precipitate with barium nitrate.

Both these salts were at first given internally (doses of 2 to 8 grains in aqueous solutions) as antipyretics, and used externally as antiseptics, especially against gonorrhœa in the form of injections and bougies. Physiological experiments have not encouraged the internal use of thalline compounds; they are poisons for the red blood corpuscles and for the nervous system (Robin, Brouardel, Loye, Weinstein, Karst).

As an injection an aqueous solution is recommended, containing 4 to 8 grains to the ounce, or a compound solution of thalline sulphate (2 to 5 per cent.) with tannin (0.2 to 0.5 per cent.) and silver nitrate (0.02 to 0.05). Towards the end of the treatment antrophores are employed containing 2 per cent. of thalline, or bougies of the same strength made up with cacao-butter.

THIOL.

Synonyms: Thiolum liquidum; Thiolum siccum.

Preparation.—Brown-colored paraffin or gas oils of specific gravity 0.890 to 0.900 are treated with sulphur at high temperatures; the unsaturated hydrocarbons, which are alone attacked by the sulphur, are extracted by suitable solvents from admixture with saturated hydrocarbons. By the action of concentrated sulphuric acid, under artificial cooling, products, soluble in water, are obtained. When the action of sulphuric acid is complete, pieces of ice are added to the mixture; thiol separates and is purified from acid and other

impurities including a peculiar odorous principle. It is then evaporated (in vacuo) to a thin extract (thiolum liquidum) or to complete dryness (thiolum siccum).

Physical and Chemical Properties.—Liquid thiol is a thin, brownish-black, neutral extract, of specific gravity 1.080 to 1.082 at 15° C., with a feeble bituminous odor reminding of birch oil; it forms clear mixtures with water, especially if glycerin be added, but is only partly soluble in alcohol and ether. Aqueous solutions, which froth abundantly when shaken, are unaffected by addition of alcohol (or by subsequent addition of dilute nitric acid), but soda, dilute acids, or metallic salts precipitate them.

When evaporated to dryness thiolum liquidum yields 40 per cent. of residue (thiolum siccum), which when further heated on platinum foil burns away with a sooty flame leaving no residue (absence of fixed alkalies). The filtrate from aqueous solutions which have been completely precipitated with nitric acid should not be rendered turbid by addition of silver nitrate (chlorine), and only assume an opalescence on the addition of barium nitrate. Petroleum ether should extract no saturated hydrocarbons from aqueous solutions. Negative results should be yielded on testing for arsenic (derived from the sulphuric acid employed) in the ash obtained by incineration with a mixture of soda and nitre.

Medicinal Uses.—Thiol was introduced into materia medica in 1888 as an addition to the armament of the dermatologist against the many forms of skin disease which come under treatment. Its advocaters recommend it as a substitute for ichthyol.

It must be included among the so-called "reducing agents" employed in dermatology, but is preferable to many of them in its relative freedom from odor and staining properties; thiol spots are readily removed from textile fabrics (Schwimmer).

The literature of thiol contains reports of its successful use in eczema, acne, sycosis, erythema, erysipelas, lymphangoitis, and generally in (a) eczematous affections, (b) acute moist inflammatory processes of the skin and subadjacent tissues, (c) chilblains and periphlebitis, (d) acute infiltration

of joints, œdema, and (e) contusions and subcutaneous hæmorrhage (Reeps, Buzzi, Neisser, Bidder, Schwimmer, Stepp). It has also been employed in a few chronic skin affections, in the ulcerous processes of syphilis, scrophulosis, lupus, in rheumatism (Schwimmer, Bidder), and in gynæcology. In the latter department of medicine it has done good service in the treatment of pelvic exudations, endometritis, etc. (Gottschalk, Kurtz). It is also recommended as a good application to burns (Bidder), and has been employed successfully in a number of parasitic skin diseases (McLaughlin), and in cutaneous eruptions of children (Moncorvo).

Thiol may be applied as powder, collodion (5 per cent. of powder), aqueous or glycerin solutions (10 to 50 per cent.), ointment (10 per cent. of the liquid), soap, plaster-mull, liniment, gelatine, etc. Internally it is given dissolved in wine (1 per cent.), as chocolate (1 to 2 per cent.), and in pills (1½ grains of the liquid each).

DERIVATIVES AND ALLIED COMPOUNDS.

Tumenol (from bi*tumen*) is a somewhat allied preparation obtained from mineral oil—freed from creosotes and acids (by soda) and from bases and pyrroloid bodies (by 70 per cent. sulphuric acid)—by the direct action of concentrated or of fuming sulphuric acid, without previous sulphuration. The product is washed free from excess of acid and forms crude tumenol.

Tumenol "venale" is a mixture of sulphones and sulphonic acids, occuring as a dark-colored acid syrup; the separated sulphones (extracted by ether from the soda-neutralized mixture) are introduced as "tumenol oil," a dark-yellow thick liquid, insoluble in water, but readily soluble in ether and benzene, and taken up by the aqueous solutions of tumenol sulphonic acid. The latter is also prepared in a separate form as a dark-colored powder, with a peculiar feebly bitter taste.

Tumenol is to be used in (1) eczema, and (2) itching of all kinds (Neisser, Fox). It does not appear to determine the absorption of exudations. Internally it has not exhibited any functional disturbances.

Externally it can be applied as a tincture (10 per cent. in ether, spir. vini rect. and water or glycerin), ointment, paste, plaster, dusting powder, etc. A 2 to 5 per cent. solution of the powder may be applied with compresses locally. The tumenol oil has been painted on the diseased surfaces undiluted.

Thiolin, or *Thiolinic acid*, is an allied preparation obtained from linseed oil by first heating 6 parts oil with 1 part sulphur to 230° C., and then treating the sulpurated oil with double its volume of concentrated acid in the warm until complete solution has taken place, when the oily product is poured into water and washed free from sulphuric and sulphurous acids. Thiolinic acid consists of a dark-green, thick extract-like mass, of faint mustard-like odor, insoluble in water, but soluble in spirit, and is recommended as a thiol and ichthyol substitute in the form of its sodium salt, a powder soluble in water. No therapeutical reports have appeared.

Phenol-sulphoricinate is a mixture of 1 part phenol with 4 parts sodium sulphoricinate, which was formerly introduced under the name of *solvine*, or polysolve, but shown to produce an analogous toxic action to saponin (Kobert). The mixture is recommended for the treatment of diphtheria (Berlioz).

Thiosapols are soaps made with fats and oils previously treated with sulphur in the cold. Employed with advantage over ordinary sulphur soaps in various skin affections (Hager).

URETHANE.

Synonym : ETHYL-URETHANE.

$$CO\begin{cases} NH_2 \\ OC_2H_5. \end{cases}$$

One of a series of compounds which may be regarded chemically as esters of carbaminic acid.

Preparation.—By the interaction of nitrate of urea and ethyl alcohol at 120° to 130° C., extraction of the resultant urethane by ether and recrystallization.

$$CO\langle^{NH_2HNO_3}_{NH_2} + HOC_2H_5 = NH_4NO_3 + CO\langle^{NH_2}_{OC_2H_5}.$$

Urea nitrate. Alcohol.

Physical and Chemical Properties.—Colorless, columnar, or tabular crystals, odorless, and with a nitrate-like taste. Readily soluble in water and in most media; the solutions are neutral. Melting point 47° to 50° C.; boils between 170° and 180° C. almost without decomposition, giving off vapors which burn with a blue flame.

Urethane yields carbon dioxide when warmed with sulphuric acid (alcohol and ammonium hydrogen sulphate being also formed), and ammonia (as well as alcohol and potassium carbonate) with caustic potash. If 6 grains are dissolved in a drachm of water, 12 grains of dried sodium carbonate with a few granules of iodine added, and the whole gently warmed, iodoform separates on cooling.

Inorganic impurities are detected by heating on platinum foil; its entire volatility also serves to distinguish it from nitre. Urea is detected, if present, by the fact that in cold aqueous solution it gives a white precipitate with nitric acid, oxalic acid, or mercuric nitrate.

Medicinal Uses.—Having been experimentally investigated as a hypnotic (Kobert and Schmiedeberg) urethane was introduced into medicine in 1885 (v. Jaksch). It was given as a sedative in mental diseases (Otto, König), and for the production of a quiet natural sleep in various cases (Riegel). It appears to produce no appreciable by- or after-effects; and with the addition of any agreeable correctives it is specially suitable for administration to children (Ewald). Good results have been yielded by it in tetanus following on injuries (Maresti), and like some others of the same class of remedies it has been credited with antidotal properties for the convulsive poisons (Anrep).

The dose of urethane is from 15 to 45 grains, in aqueous solution with correctives; subcutaneously it has been given in doses of 4 grains (Rottenbicher).

DERIVATIVES AND ALLIED COMPUNDS.

Somnal.—Under this name a solution of chloral hydrate and urethane in alcohol was introduced and employed to some extent as a hypnotic (Senator, Krafft-Ebing, Eulenberg,

Langenbuch, Brandenberg and others), but seems now to be losing popularity so far as any general use goes.

Uralium, or *Chloral-urethane.*—Chloral at ordinary temperatures, or melted chloral hydrate, dissolves urethane; if to such a solution concentrated hydrochloric acid be added it solidifies within twenty-four hours to a mass insoluble in water. This is then treated with concentrated sulphuric acid and washed with water, by which an oil results which subsequently crystallizes. The product ($CCl_3CH : OH.NHCO_2C_2H_5$) is insoluble in cold and decomposed by boiling water; it is abundantly taken up by alcohol and ether, and re-precipitated by water; melting point 103° C. Strongly recommended as a hypnotic, more reliable and better borne than chloral (Poppi). In the hands of others, on the contrary, its use was uncertain and accompanied by unpleasant secondary symptoms (Langgaard, Mairet Schmitt).

Neurodin, or *Acetyl-para-oxyphenylurethane*, $C_6H_4(OCOCH_3)NH\ COOC_2H_5$, is a colorless and odorless, crystalline substance, only slightly soluble in cold water, and in 140 parts of boiling water. It melts at 87°C. Possesses antineuralgic properties as well as an antithermic action, and has been successfully employed as an analgesic in about 30 cases of migraine, rheumatic troubles, sciatica and nervous affections, in doses of 15 grains (v. Mering).

Thermodin, or *Acetyl-para-ethoxy-phenyl-urethane*, $C_6H_4(OC_2H_5)NCO_2C_2H_5COCH_3$ occurs in odorless crystals, scarcely soluble in cold and only slightly in warm water. It melts at 86 to 88°C. It is described as a mild and reliable antipyretic, free from unpleasant effects. Employed in about 50 cases of febrile diseases, including typhus and influenza, with marked success (v. Mering). Dose, 8 to 10 grains, as powder, two or three times daily.

APPENDIX.

The compounds included in this section will be found to fall into two main classes; viz., those which are, at least at present, of insufficient importance to require detailed description in the body of the work, and those which are not purely synthetical remedies.

In no sense does it contain, or is it intended to contain all the remedies which might be met with, but only such are inserted as are thought to be of particular interest, or likely to come into demand on account of being largely recommended for therapeutical purposes. Therefore, no attempt has been made to deal with them in the form and completeness aimed at in the preceding pages, for there is great difficulty in obtaining definite information concerning many of the substances included; they are rather added for the convenience of the medical man and pharmacist than as an essential part of the book, and the information given is in most cases selected more with a view to practical usefulness than to exhaustive treatment.

ABRIN.

Nature and Source.—Active principle from the seeds of *Abrus precatorius*, Linné. A body of an albumenoid character believed to consist of two proteids, paraglobulin and α-phyt-albumose, which closely resemble snake-venom in their action and properties, except that they undergo a complete change at a temperature below boiling water.

Properties and Uses.—A brownish-yellow powder, soluble in water. It is possessed of enormous poisoning potency, $\frac{1}{100}$ of a grain being a fatal dose for a man of 130 lbs. weight; the greatest care must, therefore, be taken in its use and storage. According to Prof. Kobert abrin produces the artificial conjunctivitis for which preparations of the seed are sometimes used in ophthalmology.

ADONIDIN.

Nature and Source.—A glucoside from the herb *Adonis vernalis*, Linné.

Properties and Uses.—A yellowish-white hygroscopic powder, readily soluble in water and alcohol; insoluble in ether, chloroform and benzene. When heated above 30°C. it is converted into a brownish-black mass.

In small doses adonidin increases the vigor of cardiac action, and is stimulant and feebly diuretic; is specially indicated in aortic and mitral insufficiency, relieving the præcardial pains, dyspnœa, palpitation, etc.

Dose.—The single dose of adonidin should not exceed 1 grain; it is preferably prescribed with carbonate of ammonium and chloroform water, in doses of $\frac{1}{6}$ to 1 grain four times a day.

Adonidin tannate is a brownish-yellow powder, taken up sparingly by water and not at all by ether, but readily soluble in alcohol.

ÆSCULIN.

$C_{15}H_{26}O_9$.

Nature and Source.—A glucoside from the bark of *Æsculus hippocastanum*, Linné.

Properties and Uses.—Lustrous, white, acicular crystals, soluble in hot water, forming a solution which in the dilution of 1:1,000,000 has a blue fluorescence (especially if acidified). For this reason it has also been termed "polychrome" and "bicolorin." Æsculin has been recommended as a substitute for quinine in remittent fever.

Æscorin, a derivative of æsculin, has been employed in 10 to 20 per cent. solution by Froehlich as a diagnostic for defects in the sclerotic and conjunctiva.

AGARICIN.

Synonym: Agaric or Agaricinic Acid.

$C_{14}H_{27}OH(CO_2H)_2H_2O.$

Nature and Source.—An active principle of the fungus *Polyporus officinalis*, Fries.

Properties and Uses.—A white, lustrous powder, consisting of microscopically small crystals, tabular in form. Cold water takes up very little agaricin, but when the solvent is boiling the substance is gradually dissolved with formation of froth; on cooling separation occurs. Agaricin melts at 138° C.

The principle is somewhat widely employed as a remedy against the exhaustive night sweats of consumptives, or to combat the sudorific action of the synthetical antipyretics. It appears to be well-borne and free from any marked secondary or after-effects.

Dose.—⅓ to ½ grain, in pills (⅙ gr. in each); best taken about 6 p. m.; if the action be insufficient, the dose may be increased to 5 pills.

ALANTOL.

$C_{20}H_{32}O.$

Nature and Source.—Liquid body from the root of *Inula helenium*.

Properties and Uses.—An aromatic liquid, boiling at 200° C. It has been recommended in tuberculous diseases as a substitute for oil of turpentine.

Alant-camphor, or *Helenin*, $C_6H_{10}O$, from the same source, a neutral, colorless, crystalline substance, melting at 68 to 70° C.; on account of its antiseptic properties recommended in malaria, tuberculosis, diarrhœa, etc., in ⅙ grain doses ten times a day. Less active than alantol (Marpmann).

ALSTONINE.

Nature and Source.—An alkaloid from the bark of *Alstonia constricta*, Mueller, belonging to the Apocynaceæ.

Properties and Uses.—White, lustrous, silky crystals, which dissolve readily in ether, alcohol and chloroform; cold water does not take it up, but to hot water it communicates an intensely bitter taste.

Alstonine appears to possess antiperiodic, antiseptic and stimulant properties, combining the virtues of quinine and strychnine. Used in medicine against typhus fever.

It is also said to be used (or rather the bark) in the manufacture of pale ale, as a substitute for hops.

ANEMONIN.

$C_{10}H_8O_4$.

Nature and Source.—The active principle of the herb *Anemone pulsatilla*, Linné, and of many other Ranunculaceæ.

Properties and Uses.—Colorless, crystalline needles, which melt at 152° C. and readily dissolve in warm alcohol, whilst they are insoluble in water and ether.

Although anemonin is not to be reckoned among the powerful poisons, it is a nerve poison which acts upon the central nervous system. It is recommended in whooping cough, bronchitis and asthma, as well as in dysmenorrhœa.

Dose.—The quantity daily given varies between 1 and 2 grains, administered in two portions as powder. Larger doses must be avoided.

ANISIC ACID.

$C_6H_4(OCH_3)COOH$.

Nature and Source.—An isomer of methyl-salicylic acid, obtained by the oxidation of anethol, a constituent of anise and fennel oils.

Properties and Uses.—Colorless prisms, belonging to the monoclinic system, which melt at 180° C. and sublime unchanged. Insoluble in cold water, but freely taken up by cold and hot alcohol.

The antiseptic and antipyretic properties of anisic acid have beeen employed on the one hand in the treatment of wounds, and on the other in acute rheumatism, etc. For internal use the crystalline and readily soluble sodium salt is recommended; it has an agreeable taste and reduces the temperature without weakening the heart's power, diminishing blood pressure, or disturbing the stomach.

Dose.—Of the sodium salt 15 grains; but the preparation is very little used.

APIOL.

$C_{12}H_{14}O_4$.

Nature and Source.—A camphor from the fruits of *Petroselinum sativum,* Hoffmann.

Properties and Uses.—White needles, of a feeble parsley odor, melting at 32° C. Apiol is insoluble in water, but alcohol and ether dissolve it freely.

This substance has been used in ague as an antiperiodic, and against dysmenorrhœa.

Dose—For the former purpose 15 grains, but less for the latter.

Liquid apiol must not be confounded with this crystalline principle; it is merely an alcoholic extract of parsley seeds.

ARBUTIN.

$C_{12}H_{16}O_7$, ½ Aq.

Nature and Source.—A glucoside obtained from the leaves of bearberry, *Arctostaphylos uva-ursi.*

Properties and Uses.—Long, colorless, lustrous needles, which melt at 170° C. Cold water takes up one-eighth its weight of arbutin, while the same solvent at 100° C. dissolves an equal weight; one part is soluble in 16 parts of alcohol. Arbutin splits up when hydrolysed into hydroquinone (C_6H_4 2 OH.—See p. 149) and sugar.

Affections of the urinary tract is the special indication in which arbutin is regarded as suitable, its action being ascribed to the hydroquinone set free in its decomposition in the organism.

Dose.—75 grains *pro die* in divided doses.

ARECOLINE.

$C_8N_{13}NO_2$.

Nature and Source.—An alkaloid, isolated primarily by E. Jahns, from the seeds of *Areca catechu*, Linné, which yield at most 0.1 per cent.

Properties and Uses.—A strongly alkaline liquid, soluble in every proportion in water, alcohol, ether or chloroform; b. p. 220° C.

Arecoline is the active anthelmintic principle of areca nuts, but is also a powerful poison, affecting the heart similarly to muscarine. Its use has been suggested in veterinary practice.

Dose.—$\frac{1}{15}$ to $\frac{1}{20}$ of a grain.

ASPIDOSPERMINE.

$C_{22}H_{30}N_2O_2$.

Nature and Source.—An alkaloid isolated from the bark of *Aspidosperma quebracho*, Schlechtendal.

Properties and Uses.—Colorless, prismatic crystals, insoluble in water, but taken up by 48 parts of alcohol or 106 parts of ether.

Aspidospermine is believed to stimulate the respiratory centres and assist the oxygenation of the blood. It is recommended in asthma, dyspnœa, emphysema, etc.

Dose.—¼ to ½ grain.

ATROPINE SALTS.

$C_{17}H_{23}NO_3\bar{A}$.

Nature and Source.—Various combinations of different acidulous radicals (represented in the above formula by $\bar{A}$), with the principal alkaloid from *Atropa belladonna, Datura stramonium.* The most important are described below:

Atropine oleate is prepared by dissolving 1 part of atropine in 30 parts of oleic acid and adding 50 parts of olive oil. Regarded as similar in action to extract of belladonna, and recommended as a substitute for it in the preparation of suppositories, since they can be made with it of more uniform composition.

Atropine santoninate, a substitute for the more readily decomposed sulphate. The effects last as long as the other. Concentrated solutions must be prepared warm.

BERBERINE.

$C_{20}H_{17}NO_4$.

Nature and Source.—An alkaloid obtained from various species of *Berberis* and other plants.

Properties and Uses.—A bright yellow powder, consisting of fine lustrous needles, with a strongly bitter taste.

In the form of *phosphate*, this principle has been recommended against malaria and the digestive disturbances with vomiting of pregnancy. Other salts, especially the carbonate and sulphate, are also prepared.

Dose.— Of the phosphate, 15 grains *pro die.*

BISMUTH SALTS.

A number of organic salts of bismuth have been introduced during the past few years, and some of them have attracted more or less attention. They will be found briefly described below:

Albuminate.—A bulky, white or pale grey powder, containing up to 9 per cent. of bismuth; it has been employed with

success in America against gastric and intestinal cramps. The substance was given in daily quantities of 20 to 60 grains.

Benzoate, or *sub-benzoate*, is prepared by the interaction of an acid solution of nitrate of bismuth and an aqueous solution of sodium benzoate. A white, bulky powder, almost impalpable, used as a stimulant dusting powder in the treatment of torpid ulcers; has been specially recommended against soft chancres, a few days being sufficient to transform them into clean ulcers. The first application produces moderate burning. Recommended for internal medication in preference to the salicylate of bismuth (Vibart).

Dithiosalicylate, or *Thioform*, see under Dithiosalicylic Acid.

Naphtolate, a brownish, tasteless powder, insoluble in water; has been employed with good results in cholera in doses of 30 grains as an intestinal antiseptic, and externally as a substitute for iodoform (Schubenko and Blachstein).

Oleate was credited with emollient and mild astringent properties, and used in pustular skin affections and acne.

Oxyiodide, or *sub-iodide*, BiOI, may be obtained by a number of processes. It is a brick-red, specifically heavy powder, consisting of microscopically small, reddish, translucent, cubical crystals. Oxyiodide of bismuth is insoluble in any re-agent without decomposition. It was introduced to the notice of the medical world as an antiseptic similar in action to iodoform, but appears to have fallen short of wide favor.

Phenolate, $Bi(OH)_2C_6H_5O$, obtained by the action of bismuth chloride or nitrate on a solution of phenol in alkalies, is a gray, neutral powder, with scarcely any odor or taste, insoluble in water; used as an intestinal antiseptic in doses of 15 grains (Jarenski), and externally as an iodoform-substitute. For the *Tri bromo-phenolate* see under **Bromol.**

Pyrogallate, $[C_6H_3(OH)_2O]_2BiOH$, prepared in a similar manner to the above, is a yellow powder, recommended as an antiseptic and in dermatology, as the only bismuth antiseptic soluble in the alkaline secretions.

Salicylate, $Bi(C_7H_5O_3)_3 . Bi_2O_3$.—The *basic salicylate* of this formula is obtained by washing the so-called *acid salicylate*, precipitated from slightly alkaline solutions of sodium sali-

cylate by bismuth nitrate, with water until the washings no longer give a violet coloration with ferric chloride. It is an amorphous, yellowish-white powder, entirely insoluble in water; neither alcohol, ether, nor chloroform should extract salicylic acid from it; it should be neutral to litmus paper, and its aqueous washing should not give a violet coloration with ferric chloride. These precautions have to be taken to avoid the use of carelessly prepared compounds or mixtures containing free salicylic acid, as these have an irritant action.

Externally, the basic salicylate of bismuth has been employed in medicine as an iodoform substitute in the treatment of wounds, ulcers, etc. Internally, it has made a reputation in chronic diseases of the digestive organs and intestines. It is reported to have proved useful in diarrhœas, and in preventing fermentation in the intestines after operation. In doses of 10 to 15 grains, two or three times a day, as powder, it does not seem to cause functional disturbances, even when given for a prolonged period.

Subgallate, see under **Dermatol.**

Bismuth-cerium salicylate, a reddish-white powder, insoluble in water and alcohol. According to Salaya it is one of the most active preparations in the treatment of diseases of the gastric and intestinal mucous membrane. It is recommended particularly in diarrhœa and dysentery due to ulceration of the intestines.

BOLDIN.

Nature and Source.—Principle from the leaves of *Boldoa chiliensis*.

Properties and Uses.—This substance darkens rapidly on keeping. It is given as a tonic in liver diseases and in the treatment of biliary calculi; also in affections of the bladder, and as a hypnotic.

Dose.—3 grains daily, in capsules, or as a 5 per cent. enema.

BURSIN.

Nature and Source.—A principle from the plant *Capsella bursa-pastoris.*

Properties and Uses.—A light-yellow, hygroscopic substance, with an astringent taste. Bursin appears to be possessed of styptic properties; it has been recommended for hypodermic injection as a substitute for ergot.

BUXINE.

$C_{16}H_{21}NO_3$.

Nature and Source.—An alkaloid from the bark of *Buxus sempervirens;* probably it is identical with bebeerine.

Properties and Uses.—A crystalline mass with a very bittter taste, insoluble in water, but taken up by alcohol.

Recommended as an antifebrile.

Dose.—15 to 30 grains.

CAESIUM SALTS.

Some of the salts and double salts of caesium,—a bivalent element belonging to the group of alkali metals,—especially the bromides, have been recommended as antepileptics of more pronounced activity than the alkaline bromides. They are, however, rare and expensive, and hence have not found ready adoption into materia medica.

CAFFEINE SALTS.

$C_8H_{10}N_4O_2\bar{A}$.

Among the very considerable number of new salts of caffeine which have been made and tentatively brought under notice during the past few years, the chief are: benzoate, hydrobromide, hydrochloride, lactate, nitrate, oxalate, phenylate, phtalate, salicylate, sulphate, tannate, triiodide (*q. v.*) and valerianate. These salts are mostly of an unstable nature, and owing to the weak basic properties of the alkaloid, mostly dissociate into their constituents; or where the acid is volatile, it is gradually lost by evaporation, as in the hydrobromide.

Besides these there is also a long list of double salts, such as the citrate of caffeine and ammonium (54 per cent. of alkaloid), the benzoate, bromide, cinnamylate, citrate and salicylate of caffeine and sodium (between 45.8 and 62.5 per cent. of alkaloid), the boro-citrate, citro-benzoate, citro-salicylate. Few, if any, have succeeded in attracting attention.

The *benzoate*, *salicylate* and *cinnamylate* of sodio-caffeine are regarded as especially suitable for use subcutaneously, owing to their ready solubility.

The *boro-citrate* combines the physiological action of caffeine with the antiseptic properties of boric acid; it is readily soluble.

The *carbolate* and *phtalate* have also been recommended for hypodermic injection, being readily soluble, and even in concentrated solution without irritating effect upon the mucous membrane.

CALCIUM SALICYLATE.

$CaC_7H_4O_3,H_2O$.

Properties and Uses.—A white, crystalline powder, free from odor and taste; difficultly soluble in water. It has been recommended, either alone or in combination with bismuth salicylate, in the diarrhœa of children and in gastro-enteritis.

Dose.—8 to 24 grains.

CAMPHORIC ACID.

$C_8H_{14}(COOH)_2$.

Nature and Source.—A dibasic acid obtained by the action of nitric acid on camphor.

Properties and Uses.—White, acicular or scaly crystals, odorless, and with a feebly acid taste; m. p. 175° to 178°. Cold water takes up only little, but the same solvent hot dissolves it readily, as do alcohol and ether; also soluble in fatty oils.

Camphoric acid was first applied in 1888, in acute and chronic diseases of the respiratory tract, by Dr. Reichert, who used ½ to 6 per cent. solutions topically in angina, coryza,

acute bronchitis, etc. Several authors have cured cystitis by injections of ½ to 2 per cent. solution, and recommended it against the night sweats of consumptives. More recently Professor Schultzer and others have also recorded their conviction of the superiority of camphoric acid to other medicaments in such cases.

Dose.—Up to 30 grains.

CANNABINE.

Nature and Source.—An alkaloid isolated from the drug *Cannabis sativa*,, Linné, or Indian hemp.

Properties and Uses.—A brown, syrupy liquid, recommended as a hypnotic.

Dose.—1 to 5 grains daily.

The *tannate* of cannabine is a yellowish-brown powder, insoluble in water or ether, slightly soluble in alcohol, freely so in water rendered slightly alkaline. In doses of 2 to 10 grains, with an average of 4 grains, it has been spoken of as a useful hypnotic, especially in nervous sleeplessness and acute mania, free from unpleasant secondary effects.

CANNABINONE.

Nature and Source.—A constituent of the flowering tops of *Cannabis sativa*, Linné.

Properties and Uses.—A balsamic, resinous body, insoluble in water, but taken up by alcohol, ether, chloroform and benzene, as well as by fatty and essential oils.

Cannabinone has a hypnotic action.

Dose.—½ to 1½ grains; the taste, which is far from agreeable, may be disguised by the addition of powdered coffee.

CANTHARIDIN.

$C_{10}H_{12}O_4$.

Nature and Source.—Active principle from the entire insects of *Cantharis vesicatoria* and other allied members of the Coleoptera.

Properties and Uses.—Colorless, four-sided tables, insoluble in water, difficultly soluble in cold alcohol, more readily

in ether and in fatty oils, and most freely in chloroform; with caustic alkalies it forms salts soluble in water.

The principle has been used in place of cantharides in plasters, ointments, collodion, liquor epispasticus, etc. More recently recommended in the form of salts of cantharidinic acid with alkalies (by Liebreich) in the treatment of tuberculosis by subcutaneous injection. A similar combination with cocaine, *cocaine cantharidinate* is regarded as a mixture. The actual value of the method is still undetermined.

Dose.—1 cc. of a $^1/_5$ per mille solution.

CARDOL.

Nature and Source.—An active principle from the pericarps of *Anacardium occidentale.*

Properties and Uses.—An almost colorless oil, which gives a violet color with sulphuric acid, and with lime water a deep black color.

Medicinally cardol is used as a blistering agent.

CARPAINE.

$C_{14}H_{27}NO_2$.

Nature and Source.—An alkaloid extracted from the leaves of *Carica papaya,* Linné.

Properties and Uses.—Carpaine forms well-defined, beautiful crystals, with a very bitter taste; it melts at 121° C., and forms crystalline salts with acids.

The discoverer of the base (Greshoff) found by experiment that it was a cardiac poison; subsequent examination showed that subcutaneously it did not produce any irritation or abscess, while valuable results were produced in aortic insufficiency and stenosis, good effects being manifest within a few minutes of the injection. Recommended for the subcutaneous treatment of heart diseases. According to von Oefele it is the only substitute for digitalis that can be used hypodermically without causing any disturbance.

Dose.—$^1/_{10}$ to $^1/_6$ grain subcutaneously every day, or every second day.

CARVACROL.

$C_{13}H_{14}O$.

Nature and Source.—A phenol existent in the essential oil of *Origanum species.*

Properties and Uses.—A thick oil that does not solidify at —25° C.; b. p. 233° to 235° C.

Carvacrol possesses powerful antiseptic properties.

The *iodide* (*vide* under **Aristol**) has been employed like iodoform in substance, gauze, collodion, ointment, etc., in the treatment of wounds and skin diseases.

CATHARTINIC ACID.

$C_{30}H_{36}NO_{15}$.

Nature and Source.—A glucosidal principle from the leaves of *Cassia species.*

Properties and Uses.—Brown, hygroscopic scales, readily soluble in water and in dilute alcohol.

Therapeutically this acid is a laxative.

Dose.—4 to 6 grains, or half as much for children.

CETRARIN.

$C_{18}H_{16}O_8$.

Nature and Source.—A bitter principle from the lichen *Cetraria islandica.*

Properties and Uses.—White, acicular crystals, with a bitter taste; readily soluble in boiling alcohol.

Intravenous injections of cetrarin increase the secretion of saliva, bile and pancreatic juice, and stimulate peristalsis. Since during its use the number of blood corpuscles increases, especially when they have been diminished below the normal by disease, the principle is considered indicated in chlorosis, and has been employed by Fornaca with great success.

Dose.—Internally, 1½ to 3 grains; intravenously, ⅙ to ¼ grain per pound of body-weight.

CHROMIC ACID.

CrO_3.

Nature and Source.—The so-called chromic acid of commerce, obtained by the action of sulphuric acid upon potassium bichromate, is of course chromic anhydride or trioxide, CrO_3. The acid (the true formula of which is H_2CrO_4) is not known in the free state.

Properties and Uses.—Chromic anhydride occurs in long red rhombic needles or prisms, hygroscopic on exposure to air, and readily soluble in water. It is a powerful oxidizing agent, and in concentrated solution destroys organic matter.

Externally this compound has been used pure, or with an equal volume of water, as a caustic in the treatment of condylomata, warty excrescences, hypertrophied tonsils, etc. Its employment is also recorded as a hæmostatic in dental surgery, in dilute solution (1 to 2½ per cent.) for painting on syphilitic ulcers of the tongue, and in 5 per cent. solution against perspiration and tenderness of the feet. In the latter case the feet are carefully washed and dried, and the solution painted on; care must be taken to avoid wounded places. Also used against ozæna and gonorrhœa in 1 per mille aqueous solution.

CHRYSAROBIN.

$C_{30}H_{26}O_7$.

Nature and Source.—A principle obtained from a concretion found in the stem and branches of *Andira araroba*.

Properties and Uses.—A yellow crystalline powder, incompletely soluble in 200 parts of water, more freely in hot benzene, alcohol, chloroform, petroleum ether, strong acid and alkalies. It is used externally in the form of 10 per cent. preparations against psoriasis, herpes tonsurans, eczema, etc. It has also been recommended internally, as an emetic and aperient which acts promptly without prejudicially affecting the general well-being.

Dose.—For very young children 6 grains, for 12 years of age 9 grains, and for adults 15 grains. Generally 8 or 9 grains is a sufficient dose.

COCAINE SALTS.

$C_{16}H_{21}NO_4,\overline{A}.$

Among the number of new combinations of cocaine for which useful properties have been claimed are the benzoate, borate, cantharidinate, citrate, hydrobromide, lactate, nitrate, oleate, phenylate, phtalate, saccharinate, salicylate, sulphate, tannate and tartrate.

Only four of these need be described.

The *borate*, was recommended for eye-douches and subcutaneous injection, and said to be superior to all other cocaine salts on account of the permanence of the solution and the indifference of the acin.

The *lactate*, a white honey-like mass, easily soluble in water, is employed (Wittzack) in the local treatment of tuberculous cystitis, with lactic acid—to avoid increased sensitiveness of the bladder.

The *nitrate* is specially suitable (Lavoux) in place of the hydrochloride for prescribing in combination with nitrate of silver in the treatment of diseases of the genito-urinary tract. Even large doses of the silver salt as injection do not cause pain when associated with an equal weight of cocaine nitrate.

The *phenylate* is a thick honey-lihe mass, soluble in 50 per cent. alcohol. It has been used subcutaneously as a loca anæsthetic in dental surgery (Vian, Oefele, Vasey); as a paint or liniment (1 per cent. in 30 per cent. alcohol) in all local pain and in diphtheria; as an application in catarrhs of various mucous membranes, and in nasal and laryngeal practice (Kyle), (5 to 10 per cent. solution or powder with acetanilide). Anæsthesia appears to be produced more slowly than with the hydrochloride, but to be free from deleterious effects.

Dextro-cocaine, or *Iso-cocaine*.—The salts of this base are less soluble than those of ordinary (lævo-)cocaine and effect a more rapid anæsthesia, but are at the same time more locally irritant.

Tropa-cocaine, or *Benzoyl-pseudo-tropine*, $C_8H_{14}NO(C_7H_5O)$, a base first discovered by Giesel in the narrow-leaved Java coca, and subsequently prepared synthetically by Liebermann. Liebreich and Chadbourne find that a 3 per cent.

solution of the hydrochloride produces a more rapid anæsthesia than cocaine, whilst it is less toxic, more stable, and in other respects more advantageous. Several observers have corroborated these advantages in dental and ophthalmological practice.

CODEINE PHOSPHATE.

$C_{18}H_{21}NO_3$, H_3PO_4, $1\frac{1}{2}$ Aq.

This preparation is officially recognized in the latest edition of the Pharm. Germ.

Properties and Uses.—Fine white needles, with a bitter taste, readily soluble in water, sparingly so in alcohol; the aqueous solution has an acid reaction.

It is used in 10 per cent. solution in various mental diseases, and in the treatment of morphinism. Though an useful narcotic, codeine is not to be recommended (Pollak) for use in painful affections such as sciatica, phlegmone, etc.; it has a very good action in most affections of the respiratory organs, in certain affections of the intestinal tract, and in inflammation of the urinary canal, but has no effect upon the nervous system.

Dose.—$1\frac{1}{2}$ to 2 grains daily.

COLCHICEIN.

$C_{21}H_{22}(OH)NO_5$.

Nature and Source.—A product of the hydrolysis of colchicine (*q. v.*).

Properties and Uses.—Slightly soluble in cold, readily so in boiling water, in alcohol and in chloroform.

Colchicein is very poisonous, acting chiefly on the cerebrum and spinal column. Used subcutaneously in the treatment of gout and acute rheumatism.

Dose.—$\frac{1}{60}$ to $\frac{1}{0}$ grain hypodermically.

COLCHICINE.

$C_{21}H_{22}(OCH_3)NO_5$.

Nature and Source.—A basic principle which occurs in all parts of the meadow saffron, *Colchicum autumnale*, Linné.

Properties and Uses.—An amorphous substance, which forms a crystalline double salt with gold, and a compound with chloroform of similarly definite form. In its hydrolysis colchicein and methyl alcohol are formed. It melts at 143° to 147° C., and is readily soluble in cold water, alcohol and chloroform. Lævorotatory.

Like colchicein, the mother substance is a powerful poison; it has been recommended against gout, rheumatism, and sciatica.

Dose.—$\frac{1}{120}$ to $\frac{1}{20}$ grain.

CONESSINE.

$C_{20}H_{40}N_2$.

Nature and Source.—An alkaloid from the bark and seeds of *Holarrhena africana* and *H. antidysenterica.*

Properties and Uses.—Masses of delicate acicular crystals, which melt at 121° C.; difficultly soluble in water, readily so in alcohol, ether and chloroform.

Therapeutically, conessine seems to possess useful properties for the treatment of dysentery and diarrhœa.

CONIINE HYDROBROMIDE.

$C_8H_{17}N.HBr$.

Nature and Source.—Coniine occurs in the seeds chiefly of the hemlock, *Conium maculatum.*

Properties and Uses.—Hydrobromide of coniine occurs in crystalline form.

It reduces the frequency, duration, and intensity of the attacks of tetanus traumaticus; has also a paralyzing effect upon the respiratory muscles. The salt has been recommended subcutaneously in the treatment of cardiac asthma.

Dose.—$\frac{1}{6}$ to $\frac{1}{2}$ grain for adults, $\frac{1}{12}$ to $\frac{1}{3}$ grain for children; subcutaneously $\frac{1}{6}$ to $\frac{1}{3}$ grain.

CONVALLAMARIN.

$C_{23}H_{44}O_{12}$.

Nature and Source.—A glucoside from the lily-of-the-valley, *Convallaria majalis*, Linné.

Properties and Uses.—A whitish-brown, amorphous powder, soluble in water and alcohol.

Therapeutically, convallamarin has shown itself useful as a cardiac, resembling digitalin in action, but not cumulative.

Dose.—½ grain, gradually increasing to 5 grains.

CONVOLVULIN.

$C_{31}H_{50}O_{16}$.

Nature and Source.—The glucoside obtained from the root of *Ipomœa purga*; it is also yielded by some other plants of the same genus.

Properties and Uses.—A rubber-like, amorphous mass, with acid properties, irritant to the mucous membrane and sternutatory. Freely soluble in alcohol and acetic acid; practically insoluble in water, hot or cold.

Convolvulin is a powerful purgative.

Dose.—1½ to 3 grains.

CORNUTINE.

Nature and Source.—An alkaloid from the sclerotium of ergot, *Claviceps purpurea*, Tulasne.

Properties and Uses.—A very poisonous compound, the chemical nature of which is still uncertain; its salts are stable.

It exerts a contractile effect upon the vascular system, and is recommended in hæmorrhage from abortion, and to increase the vigor of the pains in labor. According to Prof. Kobert, cornutine is the true active principle of ergot. The citrate is also recommended by Meisels against various forms of spermatorrhœa, $\frac{1}{20}$ to $\frac{1}{10}$ grain daily effecting complete cessation of flow.

Dose.—$\frac{1}{12}$ to $\frac{1}{6}$ grain.

CORONILLIN.

$(C_7H_{12}O_6)x$.

Nature and Source.—A glucoside from the seeds of *Coronilla scorpioides*.

Properties and Uses.—A yellow pulverulent substance, easily soluble in water and alcohol.

It is a powerful poison that may be employed therapeutically (Spillmann and Haushalter) in deficient muscular energy of the heart, strengthening the pulse, increasing diuresis and decreasing œdema and dyspnœa, but is inactive in cases where digitalin is effective.

Dose.—1½ grains six times daily.

COTOIN.

$C_{22}H_{18}O_6$.

Nature and Source.—A neutral principle from the bark of species of *Nectandra*.

Properties and Uses.—A pale yellow, amorphous or crystalline powder, slightly soluble in water, freely so in ether, chloroform, alcohol and alkalies.

Cotoin is said to check salivation and night-sweats, and to have a specific action on the intestinal tract in cholera.

Dose.—½ to 2 grains dissolved in acetic ether (1:4).

CREATINE.

$C_4H_9N_3O_2$.

Nature and Source.—A natural constituent of various tissues of the animal body, especially of muscle.

Properties and Uses.—An opaque white solid, odorless, but with a bitter and acrid taste. The monohydrate occurs in transparent prisms, soluble in 70 parts of water.

Medicinally creatine has been recommended as a remedy for atony of the muscular system or digestive organs.

Dose.—1½ grains several times a day.

CUBEBIC ACID.

$C_{28}H_{30}O_7$.

Nature and Source.—A principle obtained from the fruits of *Piper cubeba*, Linn. fil.

Properties and Uses.—A white, wax-like substance, which turns brown on exposure to the air; readily soluble in alcohol and ether.

Cubebic acid is believed to be the source of the antiblennorrhagic property of cubebs.

Dose.—Up to 15 grains.

CURARINE.

$C_{18}H_{36}N$. (?)

Nature and Source.—An alkaloidal principle, which occurs as sulphate in "curare," the arrow poison of the Indians, prepared from an extract of various species of *Strychnos*.

Properties and Uses.—An amorphous substance, which gives a red color with concentrated sulphuric acid. Also in colorless, hygroscopic prisms, with a very bitter taste, readily soluble in water and alcohol, difficultly so in chloroform.

This principle is a powerful poison, which produces a general paralysing effect.

CYTISINE.

$C_{11}H_{14}H_2O$.

Nature and Source.—An alkaloid obtained from *Cytisus laburnum* and other species.

According to recent investigations, the same body is met with in *Ulex europæus*, though there it has been termed ulexine.

Properties and Uses.—In yellowish-white, deliquescent crystals; chiefly used in the form of *nitrate*, a beautiful crystalline salt, pale yellow in color, and acid in reaction.

Therapeutically cytisine stands between strychnine and curare, and has been used as nitrate subcutaneously in paralytic migraine; also diuretic in dropsy and cardiac diseases.

Dose.—$\frac{1}{20}$ to $\frac{1}{12}$ grain hypodermically.

DATURINE.

$C_{17}H_{23}NO_3$.

Nature and Source.—An alkaloid from the leaves and seeds of *Datura stramonium*, Linné, regarded as identical with hyoscyamine.

Properties and Uses.—Physically daturine exactly resembles hyoscyamine, and the analogy holds good of the physiological action upon the pupil.

The sulphate, which is generally employed, occurs in minute white granular crystals. Given to a patient suffering from acute mania it was successful in producing sleep.

DELPHININE.

Nature and Source.—An alkaloid from the seed of *Delphinium staphisagria*, Linné.

Properties and Uses.—From ethereal solutions the compound crystallizes in small rhombs, scarcely taken up by water, but freely so by alcohol and chloroform; taste bitter.

Physiologically it has a powerful action on the heart like aconitine.

Dose.—Internally 1/3 to 1 grain *pro die*.

DIGITALEIN.

Nature and Source.—A glucosidal principle or mixture from the leaves of *Digitalis purpurea*, distinguished from a number of other similar preparations by the suffix "Schmiedeberg."

Properties and Uses.—A pale yellow amorphous powder, readily soluble in water and absolute alcohol; the aqueous solution froths abundantly, probably owing to the presence of digitonin, a saponin-like substance. It is said to combine the properties of digitalin and of digitoxin (*q. v.*).

DIGITALIN.

$(C_5H_8O_2)x$.

Nature and Source.—The "digitalin verum" of Kiliani is the most closely studied und definite of the glucosidal principles of the leaves of *Digitalis purpurea*.

Properties and Use.—It is a white amorphous powder, soluble in 1000 parts water, and in 100 parts 50 per cent. alcohol, almost insoluble in chloroform and ether. In spite of its amorphous character, its individualism is proved by its constant melting point, 217° C., and the constant proportions of its crystalline hydrolytic products, digitaligenin, $C_{16}H_{22}O_2$, digitalose and grape-sugar.

According to Böhm and Pfaff, digitalin "verum" possesses the characteristic cardiac action of digitalis leaves, and is preferable in freedom from bye-effects (Mottes, Stoitcheff).

On the other hand, the digitalin of the French and Belgian pharmacopœias, although soluble in chloroform, possesses an equal and similar action, according to Bardet.

Dose.—$\frac{1}{300}$ grain every two or three hours.

Cerberin, a poisonous glucoside isolated from *Cerbera Odollam*, is, according to Zotos, a cardiac stimulant possessing the advantages of digitalin without its draw-backs.

Muawin, an alkaloidal glucoside from the bark of the Mozambique "muawi" tree. Its hydrobromide, which is adapted for subcutaneous injection, according to the pharmacological studies of Jacobsohn has qualitatively the same action of digitalin.

DIGITOXIN.

$C_{21}H_3O_7$. (?)

Nature and Source.—The most poisonous of the four or five glucosides which make up commercial "digitalin," extracted from the leaves of *Digitalis purpurea*, Linné. Practically identical with "Nativelle's crystalline digitalin."

Properties and Uses.—Digitoxin is insoluble in water, and when subjected to hydrolysis does not yield sugar, but products (toxiresin, digitalresin) which have no cardiac action, but excite clonic and tonic spasms. It occurs in white tufts of acicular crystals, with a very bitter taste; perfectly soluble in chloroform.

Dose.—$\frac{1}{2000}$ to $\frac{1}{1000}$ grain twice daily.

DIPHTHERIA ANTITOXINE.

Nature and Source.—An albuminoidal substance discovered by Behring in the blood and serous juices of animals either naturally immune to diphtheria or rendered artificially so by the gradual introduction of diphtheritic virus into the system. According to Aronson, it is best prepared from the blood of such animals by precipitating with colloid alumina, extracting the latter with dilute ammoniacal solutions, and evaporation in vacuo. Different preparations therefore appear in the market.

Properties and Uses.—The antitoxine may be obtained as a dry powder mixed with more or less inert albuminoidal matter, readily soluble in water, or as a solution. The strength of the solution is determined by the quantity required for injection to neutralize a fatal dose of diphtheritic poison in a rabbit.

The antitoxine is a natural antidote to poison generated in the system by the diphtheritic microbes, and has been successfully employed in localities where diphtheria epidemics rage, conferring a certain immunity on the individual inoculated. Within the last few months quite a number of favorable reports of its remedial and prophylactic action have appeared. In the Berlin children's hospital the serum treatment was followed by a fall in mortality from 41.7 to 13.2 per cent. (Katz). A similar reduction in the Fredrichshain infirmary consequent on the serum treatment is attributed to the mild character of the epidemic (Weibgen). Isolated cases have been reported in English medical papers where the antitoxine treatment apparently saved the patients' lives (Eastes, Still, Blomfield, Walker).

The protection afforded is quite distinct to that given by inoculation with attenuated virus as in vaccination, or with bacterial excreta as in tuberculin. It confers immediate protection, and can be employed as a remedy as well as a prophylactic, though larger quantities are required to develope its remedial virtues. As it is gradually eliminated from the system protection only extends over two or three months. The injections do not give rise to any local or general toxic symptoms.

A similar *tetanus-antiloxine* has been prepared.

DUBOISINE.

$C_{17}H_{23}NO_3$.

Nature and Source.—An alkaloid obtained from the leaves of *Duboisia myoporoides*, R. Brown; believed to be chemically identical with, or an isomer of, hyoscyamine.

Properties and Uses.—Physiologically duboisine is much stronger than hyoscyamine, and acts as a mydriatic

more rapidly than atropine and with less irritation; hence it is regarded as better suited for inflammatory affections. Requires to be used with caution. Also recommended in hystero-epileptic conditions as a hypnotic and sedative.

The *sulphate* is similar in its medicinal properties to the alkaloid; is used in solution (1 gr. to the ounce) for the eye.

Dose.—$\frac{1}{120}$ to $\frac{1}{60}$ grain internally or subcutaneously.

EPHEDRINE.

Nature and Source.—An alkaloid from the leaves of *Ephedra vulgaris.*

Properties and Uses.—Colorless, stable crystals. The *hydrochloride,* in which form the base is principally used, occurs as colorless needles, readily soluble in water.

Ephedrine has been recommended as a mydriatic in the place of homatropine. A 10 per cent. aqueous solution of hydrochloride is used for instillation into the eye, for the purposes of investigation, and a 1 per cent. aqueous solution for daily use, 2 to 3 drops being instilled into the eye several times a day

ERGOTININE.

$C_{35}H_{40}N_4O_6$.

Nature and Source.—A weak base, obtained from the sclerotum of ergot, *Claviceps purpurea,* Tulasne.

Properties and Uses.—Occurs in colorless, prismatic needles, soluble in alcohol; on exposure to light and air it rapidly darkens, absorbing oxygen. In dilute solutions ergotinine is fluorescent, with a violet color.

According to the researches of Kobert this principle, if quite pure (free from cornutin and sclerotinic acid), is inert.

ERYTHROPHLŒINE.

Nature and Source.—An alkaloid from an ordeal bark yielded by the *Erythrophlœum guineense,* a tree of the Leguminous order, found in West Africa.

Properties and Uses.—The hydrochloride of erythrophœine forms whitish crystals, soluble in water.

This alkoloid is a cardiac, said to be more powerful than ordinary "digitalin." Some years ago claims were made for it as a local anæsthetic; further investigation led to the result that the statements appear to be unfounded.

ESERIDINE.

$C_{15}H_{23}N_3O_3$.

Nature and Source.—An alkaloid from calabar beans, the seeds of *Physostigma venenosum*, Balfour, where it occurs in conjunction with eserine (physostigmine).

Properties and Uses.—Eseridine melts at 132° C. (eserine 90° C.), and is difficultly soluble in ether.

Physiologically eseridine resembles eserine, but is six times weaker in action. It has been recommended as a purgative for herbivorous animals in veterinary practice, but seems to have a tendency to act as a cardiac poison; further, if not perfectly dissolved, it may cause gangrene when subcutaneously injected.

EUCALYPTOL.

$C_{10}H_{18}O$.

Nature and Source.—An oxygenated body, first isolated by E. Jahns from the essential oil of various *Eucalyptus* species. Has also been detected in the oils of a considerable number of other plants.

Properties and Uses.—Pure eucalyptol is a colorless liquid, with a camphoraceous odor; sp. gr. 0.930, b. p. 176° to 177° C., and crystallizing point -1° C. It is practically insoluble in water, but miscible with alcohol, ether, chloroform and fatty oils. Optically the compound is inactive. It yields crystalline compounds with hydrobromic acid and with iodol under specified conditions, both of which have been employed for its detection.

Eucalyptol is generally acknowledged as the most valuable constituent of eucalyptus oil medicinally, and has been introduced into both the German and United States Pharmacopœias.

Externally eucalyptol has been used as a stimulant in rheumatism and neuralgias, and, further, in the antiseptic treatment of atonic ulcers, gangrene, etc. Internally it plays an important part in diseases of the lungs and of the respiratory system generally. The recent literature of the medicinal use of eucalyptol records its more or less successful administration in tuberculosis, pulmonary gangrene, pneumonia, irritable cough, incipient phthisis, etc. It was also very largely used during the late influenza epidemics for saturating the atmosphere with antiseptic vapor, in order to keep off attacks. There is some evidence that eucalyptol is of value in the treatment of malaria, either internally or subcutaneously mixed with oil.

Dose.—5 drops in gelatine capsules, or in emulsion, for internal administration; the same dose may be given hypodermically, mixed with oil.

Eucalypteol, a pearly crystalline substance obtained from eucalyptus oil by Anthoine is according to Voiry nothing more than terpilene dihydrochloride, $C_{10}H_{16}.2HCl$.

Eulyptol, or *Ulyptol*, is a mixture of salicylic acid, carbolic acid and eucalyptus oil.

EUONYMIN.

Nature and Source.—A resin from the root and stem-bark of *Euonymus atropurpureus*, Jacquin.

Properties and Uses.—A brown or greenish-brown hygroscopic powder, with a feebly bitter taste, soluble in water, almost insoluble in alcohol and ether.

Medicinally the dry extracts of euonymus bark, known as euonymin, are used as hepatic stimulants, being especially recommended in constipation due to hepatic torpor. Though laxative, euonymin is not nearly so active an irritant of the intestines as podophyllin.

Dose.—½ to 3 grains.

FILICIC ACID.

(AND ANHYDRIDE.)

$C_{14}H_{16}O_5$.

Nature and Source.—A principle from the rhizome of *Aspidium filix-mas*, Swartz.

Properties and Uses.—Filicic acid is a yellowish powder, consisting of microscopic, rhombic scales.

According to the most recent pharmacological investigations the crystalline filicic acid is absolutely inert (Poulson). The anthelmintic properties of male-fern extract must be ascribed to an amorphous filicic anhydride, which if absorbed into the system is distinctly toxic. As its absorption is favored by the presence of fatty oils, in which it is soluble, it is recommended not to prescribe castor oil after the extract but to select some other purgative.

FERRATIN.

Nature and Source.—The characteristic iron compound of the liver, discovered by Schmiedeberg and Marfori. Prepared artificially from albumen by heating together a solution of albumen, iron tartrate, sodium tartrate and sodium hydroxide for 2½ to 4 hours at 90° C.; the excess of alkali is then removed with tartaric acid, ammonia added, and again warmed for at least 12 hours at 90° C., when it is cooled and the iron albuminate precipitated with tartaric acid. According to Kobert and Langgaard Ferratin is not identical with the hepatin isolated from the liver by Zaleski.

Properties and Uses.—A reddish-brown powder, nearly free from taste and odor, insoluble in water and dilute acids, but readily soluble in water possessing a slight alkaline reaction. It contains about 7 per cent. iron.

On account of its occurrence in the liver, the seal of metabolic change, it is thought to be the most assimilable form in which the iron of animal food can exist. It has, therefore, been recommended as both a nutritive and remedial agent in anæmia, chlorosis and related diseases, and its use is indicated in all cases where iron has been previously employed. Clinical

results have been so far very satisfactory, general improvement and increase of hæmoglobin in the blood following its administration—which causes no digestive disturbance.

Dose.—8 grains in powder form, or 1½ to 8 grains in soluble form in milk. Children half the above doses.

GELSEMINE.

$C_{54}H_{69}N_4O_{12}$.

Nature and Source.—An alkaloid which occurs in the rhizome of *Gelsemium nitidum*, Michaux, associated with gelseminine *(q. v.)*.

Properties and Uses.—A brittle, transparent, solid mass, crystallizing with difficulty from alcohol. It fuses at 45° C. to a colorless acid liquid, which on cooling solidifies to a transparent vitreous mass; at higher temperatures it is entirely dissipated. Cold water scarcely takes it up at all, and from the same solvent hot it separates on cooling in a granular amorphous form. It forms salts, which, except the sulphate, are crystalline.

Gelsemine is regarded as the active principle of gelsemium and, hence, is credited with valuable properties in the treatment of neuralgia, toothache, convulsive cough, etc. It is said to be an antidote to strychnine.

Dose.—$\frac{1}{60}$ to $\frac{1}{20}$ grain.

GELSEMININE.

Nature and Source.—An alkaloid that is extracted together with gelsemine from the rhizome of the yellow jasmine, *Gelsemium nitidum*, Michaux.

Properties and Uses.—A dark-brown, resinous mass, permanent in the air. When powdered it has a yellow color, and a bitter taste resembling that of the rhizome. Water takes up very little, but alcohol, ether and chloroform dissolve it readily. It is a strong base, forming neutral amorphous salts with acids.

The medicinal properties of gelseminine do not seem to have been made out, or indeed its nature chemically.

GLYCERIN-PHOSPHORIC ACID.

$(HO)_2PO.O.C_3H_5(OH)_2$.

Nature and Source.—A glycerin ester of phosphoric acid, forming one of the principal components of lecithin, the most valuable phosphoric constituent of food. Prepared synthetically by the interaction of glycerin and phosphoric acid in the presence of dehydrating agents.

Properties and Uses.—A faintly yellow, odorless, oily liquid, soluble in water and alcohol, and of acid taste.

The calcium salt, $CaC_3H_7PO_6$, a white crystalline powder, easily soluble in cold water, is employed therapeutically to increase the phosphorus contents in the organism of neurasthenics and in nervous disorders. Acts antagonistic to antipyrine, and according to Dr. Robin is the active principle of testicular juice. Employed successfully in convalescence from infectious diseases and in phosphaturia, the influence on nutrition being most marked.

Dose.—4 grains, preferably injected subcutaneously.

GOLD SALTS.

Quite a number of gold compounds, salts and double salts, as well as the precipitated metals, have been introduced into medicine, such as :

Sodium auro-chloride.—A golden yellow powder, which feebly attracts moisture. It contains at least 30 per cent. of gold. Readily soluble in water, but only partly so in alcohol. Organic substance and most salts (as also light) decompose the solutions.

Like all gold preparations this double salt has been used in syphilis, either in the form of simple solutions or in lozenges with chocolate.

Dose.—$\frac{1}{6}$ to 1 grain several times a day.

Gold chloride.—Occurs in long orange crystals, very hygroscopic, readily soluble in water, alcohol and ether.

Internally this corrosive compound produces general symptoms allied to those of mercuric chloride. Externally it has been applied as powder by rubbing into the tongue

(1/6 to 1/4 grain), and as concentrated solution for the cauterizing of cancer.

Gold monobromide.—This forms a yellowish-grey, very friable mass, insoluble in water. It has been employed in Russia, Germany and Belgium as a nervine and anti-epileptic. According to some observers it is better borne than any of the bromides.

Dose.—For children 1/20 to 1/10 grain; adult dose 1/8 grain, increasing to 1/5. Against migraine 1/20 grain, twice daily, one hour before meals.

Other compounds of the metal, such as cyanide, iodide, oxide, etc., have also been tried in the treatment of syphilis, but not generally. A so-called "bichloride" was represented to be the remedy employed in the Keeley cure for drunkenness.

GUARANINE.

vide CAFFEINE.

GYMNEMIC ACID.

Nature and Source.—The active principle obtained from the leaves of *Gymnema silvestre.*

Properties and Uses.—A greenish-white, slightly astringent powder, sparingly soluble in water, easily in alcohol.

It produces a temporary ageusia towards bitter and sweet sensations, and a 12 per cent. dilute alcoholic solution is, according to Oefele, advatageously employed to rinse the mouth before taking bitter medicines, and to destroy the parageusia of diabetics.

GYNOCARDIC ACID.

$C_{14}H_{24}O_2$ (?)

Nature and Source.—The active principle from the oil of the seeds of *Gynocardia odorata*, R. Brown.

Properties and Uses.—A yellowish, unctuous solid, melting at about 30° C.; it has a burning and acrid taste, and a marked odor.

Gynocardic acid is used internally and externally, like chaulmoogra oil, in the treatment of leprosy and syphilis, and of gouty and rheumatic affections. It is regarded as superior to the oil.

Dose.—½ to 3 grains; externally as liniment with oil (1: 10 to 20).

HAEMALBUMIN.

Nature and Source.—A preparation containing the salts and albuminoidal constituents of blood in the form of acid non-coagulable albuminates.

Properties and Uses.—A stable powder, soluble in hot water and in alcoholic liquids, recommended in chlorosis and debility.

Dose.—15 grains five times a day.

HAEMOGLOBIN.

Nature and Source.—The red coloring principle of the blood.

Properties and Uses.—A doubly refractive, pleochromatic colloid or crystalline substance.

Given, owing to its content of iron in an organic and presumably easy assimilable form, in anæmia and chlorosis.

Dose.—1½ to 3 drachms daily, in wine, tablets with chocolate, etc.

It may be interesting to add that the haemoglobin of the dog has been represented by the following extraordinary formula: $C_{636}H_{1025}N_{164}FeS_3O_{181}$.

HAEMOL AND HAEMOGALLOL.

Nature and Source.—Two similar ferruginous blood preparations, introduced by Kobert as easily assimilable forms of the nutritive constituents of the blood. Haemol is prepared from neutralized blood by shaking with zinc dust and water, which have a reducing action, and subsequently removing the zinc from the precipitated zinc parahomoglobu-

lin. Haemogallol is prepared by the action of another reducing agent on the blood, pyrogallol, and subsequent removal of the excess of the reagent.

Properties and Uses.—Reddish-brown powders, insoluble in water, and practically tasteless, but easily absorbed by the system.

Employed with great success in chlorosis and anæmia, and wherever an iron medication is indicated, by a number of authors, including Busch, Kumberg, Grabe, Anselm and Porter. According to Anselm nearly the whole of the iron is assimilated by the system and produces no disturbances; and Lipstri and others found that even excessive doses caused no injury.

Zinc haemol, or haemol from which the zinc has only partially been removed, has been recommended by several authors in cases of chlorosis accompanied by diarrhœa and ulcerated stomach; being considered superior to other zinc preparations in mildness of action.

Dose.—4 to 8 grains three times daily in the form of tablets or pastilles at meal-times.

HELENIN.

C_6H_8O.

Nature and Source.—A stearoptene from the root of *Inula helenium*, Linné.

Properties and Uses.—Colorless, crystalline, neutral needles, melting at 110° C. Practically insoluble in water, but freely taken up by hot alcohol, by ether and by oils. It passes over undecomposed with the vapors of water.

Helenin has been used medicinally as a demulcent and antiseptic in whooping cough, chronic bronchitis, the diarrhœa of consumptives, etc.

Dose.—1/6 of a grain, or 6 grains *pro die*.

HELLEBOREIN.

$C_{26}H_{44}O_{15}$.

Nature and Source.—A glucoside from the rhizome of species of *Helleborus*, where it occurs in association with helleborein.

Properties and Uses.—A crystalline compound, freely soluble in water.

Helleborein has been used as a substitute for digitalis, either internally, as pills or with some viscid vehicle, or hypodermically—a mode of employment for which its ready solubility specially makes it suitable. In certain ophthalmological operations its anæsthetic action has been called into requisition, and for this purpose it is said to be superior to cocaine.

HOMATROPINE.

$C_{16}H_{21}NO_3$.

Nature and Source.—First synthetically obtained by Ladenburg from tropic acid and tropin, two derivatives of atropine. On the large scale it is a bye-product in the preparation of atropine.

Properties and Uses.—White, crystalline, readily soluble, clear prisms.

The physiological action of homatropine closely resembles that of atropine; it dilates the pupil very rapidly and energetically, but the effect passes off sooner than that of atropine. Also given against the night-sweats of phthisis. The salts chiefly employed are the *hydrobromide* (official in the B. P.), *hydrychloride*, *salicylate*, and *sulphate*.

Dose.—Homatropine is prescribed in the same doses and forms as atropine.

HYDRASTINE.

$C_{21}H_{21}NO_6$.

Nature and Source.—An alkaloid from the rhizome of *Hydrastis canadensis*, Linné.

Properties and Uses.—White, four-sided, rhombic, lustrous prisms, melting at 132° C. Also occurs in an amorphous form, and in various salts. Hydrastine is almost insoluble in water, but is taken up by ether, alcohol, and chloroform.

The alkaloid has been credited with the property of increasing the energy, number, and duration of uterine move-

ments, and therefore recommended in metorrhagia. Also internally in typhoid conditions, in dyspepsia, as an intermittent, and externally in hæmorrhoids, aphthæ, skin diseases.

The *nitrate*, which occurs in yellow crystals, melting point 120° C., and the *tartrate* of hydrastine, a yellowish-white, crystalline powder, soluble in hot alcohol and water, are also prepared.

HYDRASTININE.

$C_{11}H_{13}NO_3$.

Nature and Source.—An oxidation product of hydrastine described above.

Properties and Uses.—Acicular crystals, melting at 116° to 117° C., readily soluble in alcohol, ether, and chloroform. It forms soluble salts with most acids; the hydrochloride is most suitable for medicinal purposes, and consists of a yellowish, crystalline powder, melting at 205° to 208° C.

Two or three subcutaneous injections have been found very effective against uterine hæmorrhage, dysmenorrhœa, etc. Its prompt hæmostatic action has also been employed by Hausmann in pulmonary hæmorrhage where atropine is contraindicated.

Dose.—1 grain in 10 per cent. solution; the injections are best made in menstrual irregularities previous to the expected term. As a powder for internal administration, ⅓ grain three or four times daily.

HYOSCINE.

$C_{17}H_{23}NO_3$.

Nature and Source.—Occurs in the seeds of *Hyoscyamus niger*, Linné, associated with hyoscyamine. Hyoscine is probably identical with *scopolamine*, $C_{17}H_{21}NO_4$ (*q. v.*), or at least, according to Hesse and Schmidt, the hyoscine of commerce consists of scopolamine, though Ladenburg still maintains the existence of an alkaloid of the above composition.

Properties and Uses.—Hyoscine is itself non-crystalline; it is split up on hydrolysis into tropic acid and pseudotropine. The gold double salt melts at 196° to 198° C.

In the form of halogen salts, of which the hydrobromide is the chief, hyoscine is used as a sedative and hypnotic in various mental diseases, in asthma and neuralgias.

Hyoscine hydrobromide forms fine colorless, rhombic crystals, soluble in water and alcohol, forming feebly acid solutions, with a bitter, somewhat pungent taste.

Dose.—Internally $\frac{1}{100}$ to $\frac{1}{30}$ grain, two or three times daily, in pills or solution; subcutaneously $\frac{1}{250}$ to $\frac{1}{50}$ grain. As a mydriatic a 1 per cent. solution is employed.

INULIN.

$(C_6H_{10}O_5)_2$.

Nature and Source.—A principle from the root of *Inula helenium*, of dahlias, sun-flower, dandelion.

Properties and Uses.—A white powder, which consists of double refracting crystals, readily soluble in water and in double salts of copper and ammonia. Lævorotatory. Inulin is not fermentable by yeast, and is scarcely affected by diastase or ptyalin.

By virtue of its resistance to the action of ferments inulin has been recommended for the preparation of inulin bread for diabetics. Is also said to have proved useful as a stimulant expectorant.

Dose.—1 to 3 grains.

IODINE CYANIDE.

CNI.

Properties and Uses.—Colorless needles, with a pungent odor; difficultly soluble in water, more readily in alcohol and ether; melting point 146.5° C.

This compound of iodine and cyanogen appears to be a powerful poison to the blood and protoplasm; it is, however, much less toxic than the pure hydrocyanic acid. According to Kobert the preparation is universally destructive to the lower forms of life, and may therefore prove very useful for preserving entomological collections, taxidermic preparations, furs, and the like, from the attacks of insects, etc.

IODINE TRICHLORIDE.

ICl_3.

Nature and Source.—A compound of iodine and chlorine, prepared by passing a stream of dry chlorine gas over dry iodine crystals. Orange yellow needles, melting at 25° C. with gradual liberation of chlorine. Is completely volatile, soluble in 5 parts of water, and does not turn starch mucilage blue (free iodine).

Properties and Uses.—A powerful antiseptic and disinfectant, employed by a few authors therapeutically, but requiring caution owing to its ready decomposition.

IRON COMPOUNDS.

Properties and Uses.—The most important of the newer compounds of iron are those classed as "indifferent," such as the *albuminates*, *peptonates*, etc. According to many authors these combinations of iron, which may be regarded as probably approximating the natural forms in which the metal is present in the animal system, possess a very marked value in anæmia and chlorosis, where the prolonged administration of iron is indicated.

The indifferent preparations of iron are free from the astringency and chemical activity of iron salts as a rule, and hence have not injurious action on the teeth, nor any tendency to cause digestive disturbances. It is claimed for them that they are readily absorbed and highly active forms for the administration of iron.

KOUSSEIN.

Nature and Source.—A principle, isolated from the flowers and unripe fruits of *Hagenia abyssinica*, Willd.

Properties and Uses.—A resinoid, amorphous, yellowish crystalline powder, with a bitter, pungent taste; readily soluble in alcohol, ether, and alkalies; very little so in water.

Koussein is recommended as a substitute for cusso (kousso) as an anthelmintic.

Dose.—15 to 30 grains, divided into four doses, to be taken at intervals of half an hour. The last quantity is followed by a dose of castor oil.

LACTUCINE.

Nature and Source.—The active principle of the concrete juice (lactucarium) of *Lactuca virosa,* Linné.

Properties and Uses.—White scales, soluble in 60 to 80 parts of cold water, or in alcohol.

Lactucine has the reputation of being a sedative and hypnotic.

Dose.—1 to 5 grains.

It is worthy of note that hyoscyamine has been found (Dymond) in the extracts of various species of *Lactuca;* the properties of lactucarium may be due to the presence of this alkaloid.

LAMINE.

Nature and Source.—An alkaloid from the flowers of the dead-nettle, or white archangel, *Lamium album.*

Properties and Uses.—Lamine is credited with powerful haemostatic properties, and in the form of *sulphate* has been recommended for hypodermic injection.

LANTANINE.

Nature and Source.—An alkaloid from the herb *Lantana brasiliensis.*

Properties and Uses.—Antiperiodic and antipyretic properties have been ascribed to lantanine, and cases are recorded in which its use proved successful where quinine had failed.

Dose.—15 to 30 grains daily.

LEPTANDRIN.

Nature and Source.—A glucoside, obtained from the rhizome of *Veronica (Leptandra) virginica,* Linné.

Properties and Uses.—Leptandrin stimulates the biliary secretion and is purgative.

Dose.—1 to 3 grains as a hepatic stimulant; 8 grains produce purging without diarrhœa.

LITHIUM SALICYLATE.

$LiC_7H_5O_3, \frac{1}{2}Aq.$

Properties and Uses.—A white, crystalline powder, soluble in little more than its own weight of water; also abundantly taken up by alcohol.

According to Vulpian this salt will usefully supplement the action of sodium salicylate, as it removes the last traces of fever in acute articular rheumatism, which often obstinately resist the administration of the sodium combination. Against chronic rheumatism and rheumatic affections of the tendons it is superior to the latter.

Dose.—1 drachm daily.

LOBELINE.

Nature and Source.—An alkaloid from the herb and seeds of *Lobelia inflata*, Linné.

Properties and Uses.—A yellowish, syrupy liquid, darkening on keeping.

Medicinally, lobeline is used as *sulphate*, which, prepared from the leaves, is a yellowish-white powder, less hygroscopic than the yellowish, granular mass which is obtained from the seeds. It has been recommended in the treatment of bronchitis dyspnœa and spasmodic forms of asthma.

Dose.—1 to 6 grains, internally or subcutaneously.

MAGNESIUM SALICYLATE.

$[C_6H_4(OH)CO_2]_2Mg, 4Aq.$

Nature and Source.—This salt is prepared by the interaction, at high temperatures, of salicylic acid and magnesium carbonate.

Properties and Uses.—Long, colorless, hygroscopic crystals, readily soluble in water and alcohol, and with a bitter taste.

Magnesium salicylate was recommended by Huchard in abdominal typhus, as a valuable agent for freeing the intestinal canal from infectious substances. Even in cases where there was much diarrhœa its use is not held to be contraindicated,

as slight, laxative effects only are produced when large doses are given.

Dose.—45 grains to 1½ drachms daily, as powder, or in aqueous solution.

MANGANESE COMPOUNDS.

When manganese was found to be a natural constituent of the blood, its use was naturally suggested in anæmia and similar impoverished conditions of that fluid. Owing, however, to the insolubility of many of its compounds, and the questionable value of those primarily selected, the employment of the metal in medicine gradually fell out of use; even such soluble forms as the *chloride* and *sulphate* proved to be exceedingly liable to change. Recently, certain so-called "indifferent" preparations of manganese have been prepared and recommended for use in medicine, which may be briefly described:

Albuminate occurs as yellowish-white scales, forming, with water, a clear solution.

Saccharate is a brown powder, containing 3 per cent. of manganese; similarly soluble in water.

Other similar preparations are the "dextrinate," "mannitate" and "peptonate," but the two above described have, so far, chiefly attracted attention in the treatment of chlorotic conditions, either alone or in various combinations with the analogous indifferent preparations of iron.

MECONARCEINE.

Nature and Source.—Variously described as a derivative of narceine ($C_{23}H_{29}NO_9$), one of the rarer bases of opium, and as an arbitrary mixture of various opium constituents.

Properties and Uses.—Lemon-yellow crystals, fairly soluble in boiling water, less so in strong alcohol, but somewhat more freely in 50 per cent. alcohol. The preparation has an acid reaction, and melts, with some decomposition, at 126° C.

Meconarceine is said to have proved very effective, internally administered, in neuralgia, insomnia, morphinism and bronchitic affections.

MENTHOL.

$C_{10}H_{19}OH$.

Nature and Source.—A stearoptene, obtained from the essential oils of various species of *Mentha* growing in Japan and North America.

Properties and Uses.—Colorless, prismatic, or circular crystals, with a peculiar, peppermint-like odor; m. p. 42° C.; b. p. 212° C. Slightly soluble in water, readily in oils, in ether and in alcohol.

Menthol is anæsthetic and disinfectant. Internally it has been used as a stomachic and carminative against cardialgia, colic, the vomiting of pregnancy, as also against phthisis. Its anti-emetic property is powerful enough to stop emesis produced by ipecacuanha. Externally it has made a reputation in the treatment of neuralgias and migraine, and in the form of snuff against catarrh, ozæna. Inhalations have been adopted in influenza and pulmonary tuberculosis.

Dose.—1½ to 3 grains several times a day, in pills or spirituous solution.

Menthol benzoate is prepared by adding benzoic acid to the menthol designed for pencils; the counter-irritant effect upon the skin is increased.

Menthol carbonate, $(C_{10}H_{19})_2CO_3$, is a white crystalline powder, melting at 105° C., odorless, tasteless, and without irritant action on the mucous membranes.

Chloral-menthol is a stable, oily liquid, obtained by heating a mixture of equal parts of chloral and menthol on a water-bath, to at most 36° C. It has done good service in facial neuralgia, migraine, toothache, etc.

MERCURY COMPOUNDS.

It would be well to point out that the literature of all these compounds is very meagre; the greater number were introduced for hypodermic injection as anti-syphilitics, but no one of them seems to have as yet displaced at all generally the emulsions of calomel, yellow oxide, and mercurial ointment.

Mercuric and zinc cyanide.—This preparation, a white powder, entirely insoluble in water, was recommended by Sir J. Lister as an antiseptic, non-irritating dressing. It consisted of a certain proportion of mercuric cyanide (not exceeding 36 per cent.), the particles of which were "occluded" from the action of water by the insoluble zinc cyanide (Dunstan). In a later paper the chemist named details experiments held to prove that the preparation is a chemical compound with the formula $Zn_4Hg(CN)_{10}$. It does not seem to have given in other hands such satisfactory results as were recorded by the eminent surgeon named.

Mercuric benzoate, $(C_6H_5COO)_2Hg, H_2O$.—Small crystals, free from color, taste, and odor, sparingly soluble in cold, more readily in hot water, and in alcohol. In solution in brine, or suspended in liquid paraffin, was used by Stukowenkow subcutaneously against syphilis, and also by Cochery, one syringeful daily being given of a solution of the benzoate, sodium chloride and water, in the respective proportions 3:1:400. If cocaine were added, in order to relieve the slight pain of the injections, it would produce a separation of mercury.

Mercuric carbolate or *phenylate*, $(C_6H_5O)_2Hg$.—Occurs as colorless needles, practically insoluble in water and cold alcohol, but taken up by hot alcohol (1:20), by ether, or a mixture of alcohol and ether, and by glacial acetic acid. Used against syphilis by Schadeck, in doses of ⅓ to ½ grain (children $\frac{1}{15}$ to $\frac{1}{12}$ grain) twice or three times a day.

Mercuric formamidate is a solution obtained by the action of formamide upon mercuric oxide. It does not coagulate albumen, is rapidly absorbed, and excreted with the urine.

Mercury gallate has been recommended as a substitute for the tannate, which is very unstable. It is a dull, greenish-black preparation, obtained by the interaction of molecular quantities of yellow mercuric oxide and crystalline gallic acid in paste form. An anti-syphilitic, without the disagreeable characters of the chloride or subiodide.

Mercuric imido-succinate or *asparaginate*, $[C_2H_4(CO)_2N]_2Hg$. First described in 1852 by Dessaignes, and recommended by v. Mering and Vollert in 1888 as an antisyphilitic. It forms a white, lustrous, crystalline powder, which gives a clear

solution with 25 parts of water, or 300 parts of alcohol. Subcutaneously injected in doses of $\frac{1}{5}$ grain. An addition of cocaine can be made without decomposing the salt.

Mercuric naphtolate.—A lemon-yellow powder, odorless, insoluble in water; contains 30.8 per cent. of mercury. The dose for internal administration is 1 grain. Naphtolacetate of mercury (similar in constitution to thymolacetate, *q. v.*) is a white, crystalline substance. These compounds were tried by Jaddasohn and Zeissing, but found to produce more violent pain than the thymolacetate or salicylate of mercury.

Mercuric oxycyanide, $Hg_2O(CN)_2$, has been spoken highly of as an antiseptic by Boer, according to whom it is superior to sublimate as a germicide, while it is neutral, does not coagulate albumen, is less caustic, and does not attack instruments so powerfully.

Mercuric peptonate.—A yellowish liquid, with a saline, feebly metallic taste, and slight acid reaction. Was introduced as a mild and efficient mercurial for hypodermic injection, not causing pain, nor producing abscesses. The usual dose was given as 1 ccm., said to correspond to $\frac{1}{6}$ grain of mercuric chloride. A modification of this preparation has been quite recently brought under medical notice; *viz.*,

Glutine-peptone sublimate, described as a double compound of glutine peptone hydrochloride (made by the action of hydrochloric acid on gelatine) with sublimate, containing 25 per cent. of the latter. It forms a white, lustrous powder, hygroscopic, but very stable; is almost solely offered in the form of 1 per cent. solution. The dose used by Dr. Hüfler was a Pravaz syringeful of solution, which corresponded to about $\frac{1}{6}$ grain of mercuric chloride. The injections were described as accompanied by little pain and no severe local symptoms, while rapid and efficient in action on the disease. It is, according to Eichhorn, the promptest and most effective of the mercury preparations in the treatment of syphilis.

Mercury potassium thiosulphate, $3\,Hg(S_2O_3)_2 + 5\,K_2S_2O_3$, a crystalline double salt of mercury and potassium, obtained by dissolving yellow mercuric oxide in a solution of potassium hyposulphite. Its injections are free from any local or irritant

action according to Dreser and Camerer, and its solutions do not precipitate albumen.

Mercury pyroborate, HgB_4O_7, is a fine, amorphous, brown, powder, neither soluble in alcohol nor in water. It has been recommended for the treatment of wounds, and is said to have given good results.

Mercuric salicylate, $C_6H_4OCO_2Hg$.—A fine, white, neutral powder, free from odor or taste, forming soluble double salts with the halogen chlorides, bromides, or iodides. It was first recommended in 1887 by Silva-Aranjo, and later by Schadek, as a mild but energetic mercurial for internal and external use. Internally the dose was $\frac{1}{60}$ to $\frac{1}{8}$ grain, chiefly in pill form; externally it was prescribed in 0.4 per mille solution as an injection in gonorrhœa, and suspended in mucilage for intra-muscular injection. Has perhaps been more widely used than any other of the newer compounds of mercury, having the advantage of convenience in use, absence of poisoning symptoms, and promptness of action; it seems, however, to be inferior in reliability of effect to some other mercurials.

Mercury sozoiodol (*v.* Sozoiodol).

Mercury tannate.—Somewhat dull, brownish-green scales, free from odor and taste; yields tannin to water or alcohol, but is not *per se* soluble in these liquids. Was recommended as an anti-syphilitic by Lustgarten, its beneficial action being ascribed to its decomposition by the alkaline fluids of the intestine, metallic mercury being set free. Dose 1 to 2 grains, half to one hour after food.

Mercuric thymolate, $(C_{10}H_{13}O)Hg\text{-}HgNO_3$.—When pure, this compound, first recommended in England, is said to be perfectly colorless and free from odor, though on exposure it gradually becomes reddish, and acquires a faint thymoloid odor. The so-called *thymolacetate* of mercury has the formula $(C_{10}H_{13}O)Hg\text{-}HgC_2H_3O_2$. Both these compounds (as also a "thymolsulphate") were examined by Kobert, and shown to be suitable for therapeutical use against syphilis; chiefly the thymolacetate was employed, in doses of $\frac{1}{12}$ to $\frac{1}{6}$ grain, internally, as pill, or for intra-muscular injection, suspended in paraffin. Pain and infiltration were rare. The administration

of thymolacetate of mercury by intra-muscular injection, with the simultaneous internal administration of potassium iodide, has also been warmly recommended in the treatment of pulmonary tuberculosis; this method (described by Tranjen) seems to be specially useful in the earlier stages of the disease, and without ill effects even when it is far advanced.

MORPHINE SALTS.

$C_{17}H_{17}(HO)_2.NO,\overline{A}.$

Anisate. A white, crystalline powder, soluble in water, less so in alcohol.

Benzoate. A white, neutral powder, soluble pretty freely in hot water (about 1 : 5). From the hot, saturated solution the salt crystallizes in hard prisms on cooling. Recommended in the same doses as morphine hydrochloride against asthma.

Borate. This preparation has been suggested for subcutaneous injection, on account of its stability, and for eye-washes, owing to the harmlessness of the boric acid.

The hydrobromide, phtalate and saccharinate have been described, but are scarcely to be regarded as permanent additions to materia medica.

MUSCARINE.

$C_5H_{15}NO_3.$

Nature and Source.—An alkaloidal principle, obtained from the fungus *Agaricus muscarius*.

Properties and Uses.—A hygroscopic, crystalline substance, readily soluble in alcohol.

Muscarine is a powerful poison, and physiologically an antidote to atropine.

MYRTOL.

Nature and Source.—A fraction of the oil of *Myrtus communis*, boiling between 160° and 180° C.

Properties and Uses.—A clear liquid, of not unpleasant odor, recommended (Eichorst), to be taken twice a day, as a

reliable and prompt remedy against pu.r.d processes of the respiratory tract. According to E. Jahns, myrtol is a mixture of dextro-pinene and eucalyptol, and would be advisedly replaced by the latter.

Dose.—5 minims.

NICOTINE BITARTRATE.

$C_{10}H_{14}N_2(C_4H_6O_6)_2$.

Nature and Source.—A salt of nicotine, the liquid alkaloid ($C_{10}H_{14}N_2$) which is found as malate in the leaves of *Nicotiana tabacum*, Linné.

Properties and Uses.—Fine, white crystals, with a tendency to aggregate; readily soluble in water. The salt is stable, and keeps well even in solution.

This salt is recommended as the most suitable form of administering nicotine in tetanus, strychnine poisoning, etc.

ORMOSINE.

Nature and Source.—An alkaloid, obtained from the seeds of *Ormosia dasycarpa*, a papillionaceous plant of Venezuela.

Properties and Uses.—Small, white crystals, insoluble in water and in dilute alkalies, readily soluble in alcohol and chloroform; melting point 80° C.

Ormosine resembles opium in its physiological action, but has not been accurately studied.

OSMIC ACID.

OsO_4.

Nature and Source.—Metallic osmium, as finely divided as possible, is heated to about 400° C., and the volatile tetraoxide caught in cooled receivers.

Properties and Uses.—Lustrous, transparent, yellow needles, with an unbearable penetrating odor (the vapor is poisonous); boiling point about 100° C. Forms a solution with water, which has an intense burning taste.

Osmic acid has been employed subcutaneously in neuralgia, goitre, canceroid and scrofulous ulcers, and internally against epilepsy.

Dose.—$\frac{1}{50}$ grain in pills, subcutaneously employed in the form of 1 per cent. solution, which should be always freshly prepared.

OUABAIN.

$C_{30}H_{46}O_{12}$.

Nature and Source.—A glucoside from the wood of *Acocanthera ouabaio*, an apocynaceous tree of the Somali coast; also obtained from the seeds of *Strophanthus glabrus*, from Gaboon.

Properties and Uses.—White, odorless crystals, with a feebly bitter taste, little soluble in cold, readily in hot water and spirit; insoluble in chloroform, absolute alcohol and anhydrous ether. Melting point 200° C.

Ouabain has been internally used in the whooping cough of children; the attacks are diminished in number and intensity.

Dose.—For children, $\frac{1}{100}$ grain every three hours.

OXYSPARTEINE.

$C_{15}H_{24}N_2O$.

Nature and Source.—An oxidation product of sparteine (*q. v.*), occurring in white, hygroscopic needles, that melt at 83° C., dissolve in alcohol, water, chloroform and ether, yielding strongly alkaline solutions.

Properties and Uses.—The base possesses a stimulant action on the heart though slowing the pulse. The *hydrochloride* is recommended by Oefele for subcutaneous injection in cardiac failure, especially when accompanied by muscular degeneration. Action annulled by opiates.

Dose.—$\frac{3}{5}$ grain, increasing to 1½ grains, in 10 per cent. solution once a day.

PAPAIN.

Nature and Source.—An enzyme from the juice of the unripe fruit of *Carica papaya*, Linné.

Properties and Uses.—An amorphous, whitish powder, very liable to change. Like the animal ferments, it has the power of digesting albuminous substances, with the difference that it is active in acid, alkaline and neutral solutions.

Therapeutically papain is used internally as an aid to digestion, in dyspepsia, gastric and intestinal catarrh, and generally where there is an insufficiency of gastric juice. It is also credited with valuable galactagogue properties, but since it seems to have an abortifacient action its administration requires care. Is further reported to be of service as an anthelmintic. Externally it finds extensive application topically for the removal of the false membranes of croup and diphtheria, and in the treatment of certain indurated diseases of the skin.

Dose.—1½ to 8 grains, in pill, powder, wine or syrup.

PANCREATIN.

Nature and Source.—One of the digestive enzymes, or a mixture of several, extracted from the pancreatic juice of the pig or calf.

Properties and Uses.—Pancreatin occurs in the form of solid and fluid extracts. It hydrolyses starch, forming sugar, and in alkaline solution, peptonizes albumen and emulsifies fats. Recommended as a digestive agent *per os*, and as an addition to nutrient enemata, as also for the preparation of peptonized milk, which is often well borne by patients with weak digestion when all other forms of food cannot be retained.

Dose.—From 15 grains to 3 drachms or more, according to the nature of the preparation selected.

PAPAVERINE HYDROCHLORIDE.

$C_{20}H_{21}NO_4.HCl$.

Nature and Source.—The hydrochloric acid salt of one of the opium alkaloids, occurring in white, rhombic needles, soluble in 100 parts cold water.

Properties and Uses.—Formerly employed as a hypnotic; recently, in consequence of its sedative action on in-

testinal movements and freedom from the bye-effects of morphia and opium, it has been employed by Leubuscher in diarrhœa, especially of young children, with great success.

Dose.—$\frac{1}{12}$ to $\frac{3}{4}$ grains, in powder or in syrup, two or three times a day.

PARACOTOIN.

$C_{19}H_{12}O_6$.

Nature and Source.—A principle obtained from the so-called para-coto bark produced by a Bolivian tree, possibly *China coto.*

Properties and Uses.—A bulky, light-yellow, crystalline powder, free from odor and taste, difficultly soluble in water and ether, more readily in alcohol.

This principle, like the closely allied cotoin, has been enthusiastically recommended as an anti-diarrhœic. Being antiputridic and antiseptic, it has a beneficial effect in simple catarrhs of the stomach and intestines, in the diarrhœa of consumptives, and in cholera nostras. Its action has also been praised in the sweats of consumptives.

Dose.—2 to 3 grains, in mixture or as powder.

PELLETIERINE.

$C_8H_{15}NO$.

Nature and Source.—An alkaloid from the root-bark of *Punica granatum,* Linné.

Properties and Uses.—A colorless liquid, soluble in 20 parts of water; miscible in all proportions with alcohol, ether and chloroform. It forms crystalline salts with acids, of which the chief are, the

Sulphate, a thick liquid substance; and the

Tannate, a yellowish, pulverulent compound, with an astringent taste, soluble in about 700 parts of water and 80 parts of alcohol.

A *hydrobromide* and *hydrochloride* are also prepared.

These combinations have a reputation as anthelmintics.

Dose.—5 to 6 grains, followed in half an hour by a laxative (senna or jalap.)

PEREIRINE.

Nature and Source.—An alkaloid from the bark or root-bark of *Geissospermum lævе* (Pao Pereiro), a member of the order Apocynaceæ.

Properties and Uses.—Has a tonic action, similar to that of gelsemine, but is also antifebrile. Has been used in the form of salts against malarial fever.

Valerianate.—A brown, crystalline powder, readily soluble in alcohol, difficultly so in water, insoluble in ether. A *hydrochloride* is also prepared.

Dose.—Up to 30 grains, given some hours before the expected attack.

PHLORIDZIN.

$C_{21}H_{24}O_{10}$.

Nature and Source.—A glucoside, from the root bark of various trees belonging to the order Rosaceæ.

Properties and Uses.—Long, silky needles, or tufts of needles, sparingly soluble in cold water, but freely taken up by that solvent at 100° C., and by alcohol; m. p. 106 to 108° C., losing water; becomes solid again at 130°, and melts a second time at 170 to 171° C.

Phloridzin produces artificial diabetes in the animals to whom it is given; 8 grains per pound of body weight causes an excretion of sugar, lasting 24 to 30 hours, and amounting to 1½ to 3 drachms. It is employed in physiological research.

PHOTOXYLIN.

Nature and Source.—A nitro-cellulose, prepared from wood-wool.

Properties and Uses.—Soluble in a mixture of equal parts of ether and alcohol, and otherwise very similar to pyroxylin. A 3 to 5 per cent. solution is a thick liquid, which on evaporation leaves a much stronger film than collodium does. Photoxylin is employed in plastic surgery.

PHYSOSTIGMINE.

$C_{15}H_{21}N_3O_2$.

Nature and Source.—An alkaloid from the seeds of *Physostigma venenosum*, Balfour.

Properties and Uses.—The physical and chemical properties of the alkaloid are well known. More recently two salts have been prepared and brought under medical notice; both are official in the Pharm. Germ. III.

Salicylate.—Colorless, or feebly yellow, lustrous crystals, which dissolve slightly in water (1:150), and in alcohol (1:12); the solutions are neutral to litums. The dry salt is stable, but the aqueous and spirituous solutions soon assume a reddish color.

Sulphate.—A white, somewhat hygroscopic, crystalline powder, which dissolves readily in water and alcohol; the solutions are neutral to litmus.

The salicylate is chiefly used in ophthalmology (⅓ to 1:150 of water), but also internally in convulsive affections, in intestinal atony, and as an antidote to atropine.

The sulphate is used in veterinary practice, subcutaneously, against colic.

Dose.—Of the salicylate, internally, $\frac{1}{100}$ to $\frac{1}{50}$ grain; of the sulphate, for horses and cattle, 1½ grain.

PICROPODOPHYLLIN.

Nature and Source.—A neutral principle, from the rhizome of the *Podophyllum peltatum*, Linné.

Properties and Uses.—A crystalline body, regarded as the chief constituent of podophyllin.

Picropodophyllin is credited with laxative and hepatic properties.

PICROTOXIN.

$C_{12}H_{16}O_7Aq$.

Nature and Source.—A bitter principle, obtained from the fruits of *Anamirta cocculus*, Wight and Arnott.

Properties and Uses.—Colorless, lustrous, bitter nedles, soluble in alcohol, less so in water and in ether.

Medicinally picrotoxin is used against spinal paralysis, and in the night-sweats of consumptives; externally in skin diseases and as an antiparasitic.

Dose.—$\frac{1}{100}$ to $\frac{1}{10}$ grain. Externally, applied as ointment (3 to 5:250 of fat).

PILOCARPINE.

$C_{11}H_{16}N_2O_2$.

Nature and Source.—An alkaloid isolated from the leaves of *Pilocarpus pennatifolius*, Lemaire, and regarded as belonging to the nicotine group.

Properties and Uses.—The alkaloid itself is a non-crystallizable, soft, viscous mass, very slightly soluble in water, feebly so in ether, in alcohol and in chloroform. Chiefly used as

Hydrochloride, which occurs in white microscopic crystals, readily soluble in water and alcohol, but less so in ether and in chloroform.

Mechanically pilocarpine salts are used externally, by hypodermic injection, as diaphoretics in diseases of the respiratory tract, dropsies, scarlatina, diphtheria, rheumatic affections, certain skin affections, etc. The injections may produce collapse and pulmonary œdema. Regarded as an antidote to ether. Also used to strengthen the hair, in pomades and washes.

Dose.—⅓ grain or ½ grain pro die.

PIPERINE.

$C_{17}H_{19}NO_3$.

Nature and Source.—An alkaloid from the fruits of *Piper nigrum*, Linné.

Properties and Uses.—When pure, piperine is colorless, and has little or no pungency; mostly more or less contaminated with resin, and then yellowish and pungent. Practically insoluble in cold or hot water, or in ether; fairly soluble in alcohol; freely so in sulphuric and acetic acids.

Given internally as a laxative and antipyretic.

Dose.—1 to 10 grains, several times a day, in powder or pills.

PIPERONAL.—(Heliotropin.)

$C_8H_6O_3$.

Nature and Source.—When the alkaloid piperine is boiled with alcoholic potash, potassium piperate crystallizes out in lustrous prisms. By oxidation of piperic acid ($C_{12}H_{10}O_4$) piperonal is obtained.

Properties and Uses.—Small, white crystals, soluble in alcohol and ether; insoluble in water.

Is antiseptic and antipyretic. Its chief employment, however, is in perfumery.

Dose.—Up to 15 grains every three hours.

POTASSIUM COMPOUNDS.

Among the long list of combinations which might be classed under this head, only two or three require detailed mention.

Auro-cyanide, $KAuCy_4$.—White crystals, soluble in water. Subcutaneously injected is rapidly absorbed; does not precipitate albumen.

According to Behring's researches, 1 part of this compound in 25,000 parts of blood serum rendered the latter unsuitable as a medium for the growth of anthrax bacilli. The allied *mercuro-cyanide* (K_2HgCy_4) effects the same in a dilution of 1:60,000.

Cantharidate.—Used hypodermically by Liebreich in very attenuated solutions in the treatment of tuberculosis (*v.* Cantharidin).

Cobalto-nitrite, $K_6Co_2(NO_2)_{12}$. 2 Aq.—Yellow microscopic crystals, very little soluble in cold water; insoluble in alcohol and in ether.

Recommended in cases where nitrites are considered indicated, *e. g.* in dyspepsia, cardiac albuminuria, etc. Has been claimed to be more easily regulated in its physiological action than most nitrites. Dose.—½ grain every two or four hours.

Mercuro-cyanide, *v.* Auro-cyanide.

Osmate.—A violet-red crystalline powder, soluble in water. Employed in combination with bromides against epilepsy, and

subcutaneously in neuralgias, goitre and neuralgia (*v.* also Osmic acid). **Dose.**—$\frac{1}{60}$ grain; $\frac{1}{40}$ grain *pro die.*

Sozoiodol. (*v.* Sozoiodol).

Tellurate, K_2TeO_4.—A white crystalline salt, soluble in water. Has been given in phthisis, with the effect of reducing and even arresting the night sweats. Does not alter the course of the disease. Communicates an intense garlic odor to the breath.

QUASSIIN.

$C_{41}H_{42}O_9$.

Nature and Source.—An indifferent, bitter principle, from the wood of *Picraena excelsa* and of species of *Quassia.*

Properties and Uses.—A crystalline body.

Recommended as a stomachic and tonic for the stimulation of digestion and secretion.

Dose.—$\frac{1}{30}$ to $\frac{1}{3}$ grain.

QUEBRACHINE HYDROCHLORIDE.

$C_{21}H_{26}N_2O_3 . HCl$.

Nature and Source.—Salt of an alkaloid from the bark of *Aspidosperma quebracho,* Schlecht.

Properties and Uses.—Internally and subcutaneously in the treatment of dyspnœa.

Dose.—1 to 2 grains.

QUINIDINE TANNATE.

$(C_{20}H_{24}N_2O_2)_2C_{27}H_{22}O_{17}$.

Nature and Source.—An alkaloidal salt, obtained from the bark of *Cinchona pitayensis,* and other species.

Properties and Uses.—An almost tasteless salt. Has been given in dyspepsia, diarrhœa, nephritis and albuminuria. Also recommended in veterinary practice.

Dose.—3 to 12 grains, two to four times daily.

QUININE SALTS.

The number of new quinine combinations is very considerable, but it is very doubtful whether more than one or two of them will obtain a permanent place in materia medica. Following is a full list:

Quinine albuminate.
" ammonio-citrate.
" arsenate.
" borate.
" dihydrobromide.
" dihydrochloride.
" dihydrochl. carbamate
" ethylsulphate.
" ferri-chloride.
" ferri-cyanide.
" ferro-citrate.
" ferro-cyanide.
" ferro-peptonate.
" ferro-salicylate.
" glycyrrhizin.
" hydrobromide.
Quinine hydrochl.-citrate.
" hydrochl.-sulphate.
" hydrofl.-citrate.
" hydrofl.-silicate.
" iodo-hydroiodide.
" lactate.
" oleate.
" peptonate.
" phenylate.
" phenylo-muriate.
" phenylo-sulphate.
" phtalate.
" saccharinate.
" salicylate.
" tannate.

The *Ferri-chloride* occurs in dark-brown, lustrous scales, or as a reddish-brown, hygroscopic powder, with a bitter, astringent taste; readily soluble in water and in 70 per cent. alcohol.

It has been recently recommended as an excellent haemostatic, well suited for internal or external use. It may be strewn on bleeding surfaces, snuffed in epistaxis, and applied in 2 per cent. solution in uterine haemorrhage. Internally has been given in gastro-intestinal bleeding and in hæmoptysis.

Dose.—1½ to 3 grains several times a day, in pills, wafers or mixture.

Hydrochlorsulphate, $(C_{20}H_{24}N_2O_2)\,2HCl, H_2SO_4 + 3H_2O$.—This salt is recommended for subcutaneous injection, by Grimaux and Laborde, on account of its solubility in equal parts of water. It contains the same actual percentage of quinine as the sulphate.

Oleate.—A greyish-yellow, granular mass, forming a clear solution in alcohol.

Employed in skin diseases, etc., in the form of ointments, suppositories and the like.

Salicylate.—Fine, white needles, difficultly soluble in water, more readily so in alcohol.

This salt combines the properties of quinine and salicylic acid, and hence is considered indicated as an antiseptic and antipyretic in typhus, articular rheumatism, etc.

Dose.—1½ to 8 grains.

Tannate.—Obtained by precipitation of a solution of quinine with tannin; is a yellowish-white, amorphous powder, of very slightly bitter and astringent taste, containing 30 to 32 per cent. quinine, and is sparingly soluble in water.

Employed in diarrhœa, whooping-cough, night sweats and as a roborant.

Dose.—3 to 8 grains thrice daily.

QUINOIDINE.

Nature and Source.—A mixture of amorphous alkaloids, obtained as a bye-product in the manufacture of the crystallizable principles of cinchona bark.

Properties and Uses.—A brownish-black mass, insoluble in water, unless the latter be made feebly acid; has a nauseous taste. The two salts named below are also used.

Borate.—A cheap quinine substitute (8 to 15 grains pro dosi).

Citrate.—A brown, hygroscopic mass, soluble in two parts of hot water, also in alcohol, glycerin and acids.

Dose.—The same as that of quinine.

RETINOL.

Nature and Source.—A product of the destructive distillation of resin.

Properties and Uses.—A yellowish, oily liquid, which boils at temperatures above 280° C.

Retinol is a useful solvent for a large number of the newer remedies, *e. g.*, iodol, aristol, cocaine, as well as of carbolic acid, creosote, phosphorus, and many alkaloids. The solution of phosphorus is very stable, and has been recommended for the external and internal use of the metalloid.

RUBIDIUM AMMONIUM BROMIDE.

$RbBr(NH_4Br)_3$.

Properties and Uses.—A white, crystalline powder, readily soluble in water; its taste is cooling and saline.

This double salt of rubidium was recommended as a substitute for potassium bromide in epilepsy, having the advantage of a more marked sedative action. It has failed, however, to attract attention.

Dose.—1 to 2 drachms daily, in mixture with lemon syrup.

RUBIDIUM IODIDE.

RbI.

Properties and Uses.—Colorless crystals, readily soluble in water, possessing most of the characteristics of potassium iodide.

The therapeutical employment of this salt of a comparatively rare metal has been recently promoted by the discovery of a new process of recovering it from the Stassfurth salts. Indications for use are the same as for potassium iodide, but quite a number of authors have pointed out its advantage in clinical practice, namely, a minimized action on the heart, absence of gastric disturbance and a milder taste. Its administration can consequently be continued in many cases where the potassium salt must be abandoned, and in the treatment of syphilis, skin diseases and ophthalmic disorders good results have been obtained.

Dose.—2 grains 3 times daily, in milk; 5 per cent. solution as an eye lotion.

SANGUINAL.

Nature and Source.—A preparation of fresh blood, defibrinated and evaporated, and said to contain 44 parts blood-salts, 10 parts oxyhæmoglobin, and 46 parts peptonized muscle albumin.

Properties and Uses.—The preparation occurs only in pill form, each of which are supposed to represent 1¼ drachm of fresh blood, and on account of its containing the natural iron and manganese salts of the blood it is recommended in the treatment of chlorosis, etc.

SANGUINARINE NITRATE.

$C_{17}H_{15}NO_4HNO_3$.

Nature and Source.—The salt of an alkaloid, obtained from the root of *Sanguinaria canadensis*.

Properties and Uses.—A stimulant and tonic, in large doses purgative and emetic; also an expectorant.

Dose.—$\frac{1}{12}$ to ⅛ grain as an expectorant; ½ to 1 grain as an emetic.

SANTONINOXIM.

$C_{15}H_{18}O_2NOH$.

Nature and Source.—A derivation of santonin, obtained by the action on the latter of hydroxylamine hydrochlorate in alcoholic solution under the addition of soda.

Properties and Uses.—White crystals, soluble in alcohol and ether, only difficultly so in water, or in weak alkaline and weak solutions; m. p. 162° C.

Santoninoxim is said to be less poisonous than santonin, and is therefore recommended as an anthelmintic; the desired effect is produced without any functional disturbance.

Doses.—For children of 2 to 3 years, 1 grain.
" " " 4 to 6 " 1½ "
" " " 6 to 9 " 2 "
" adults 5 "

divided into two portions, with an interval of 1 to 2 hours, followed by a purgative. Must be repeated for 2 to 3 days, one after the other.

SCILLAIN.

Nature and Source.—A glucoside from the bulb of the squill, *Urginea scilla*, Steinheil.

Properties and Uses.—A colorless or yellowish bulky powder, which forms a red solution in hydrochloric acid.

The compound is diuretic and toxic, resembling the digitalis glucosides.

Dose.—$\frac{1}{60}$ grain, or $\frac{1}{6}$ to $\frac{3}{4}$ grain *pro die.*

SCILLIPICRIN.

Nature and Source.—A principle from the bulb of *Urginea scilla.*

Properties and Uses.—An amorphous, yellowish-white, very hygroscopic powder, readily soluble, and suitable for hypodermic injection.

Scillipicrin is a powerful diuretic, which reduces the activity of the heart.

Dose.—$\frac{1}{60}$ grain.

SCLEROTIC ACID.

$C_{12}H_{19}NO_9$.

Nature and Source.—A principle obtained from the sclerotium of *Claviceps purpurea*, Talasne.

Properties and Uses. — A faintly acid, hygroscopic powder, free from taste and odor; readily soluble in water, difficultly so in alcohol.

Sclerotic acid has been recommended for injection as a substitute for extract of ergot, and also in the treatment of epilepsy. Is inferior to cornutin in gynæcology.

Dose.—½ grain; 5 grains *pro die.*

SCOPARINE.

Nature and Source.—A principle from the tops and twigs of *Cytisus scoparius*, Link.

Properties and Uses.—A feebly acid substance.

Scoparine is diuretic.

Dose.—8 to 15 grains internally, or ½ to 1 grain subcutaneously.

SCOPOLAMINE.

$C_{17}H_{21}NO_4$.

Nature and Source.—An alkaloid from the roots of *Scopolia atropoides*, and very probably identical with the hyoscine of *Atropa Belladonna*, and isomeric with or closely analogous to atropine and hyoscyamine.

Properties and Uses.—Physiologically investigated by Kobert and practically tried by Raehlmann, it was found to be similar in action to the above alkaloids, and according to the latter investigator, superseded all other tropeines in its use as mydriatic and antiphlogistic. Employed as *hydrobromide*, $C_{17}H_{21}NO_4\,HBr + 3\,H_2O$, an easily soluble crystalline salt. In his experience and that of subsequent investigators scopolamine is about 4 to 5 times as strong a mydriatic as atropine and, prescribed in 1 to 2 per mille solutions, is free from the unpleasant effects of the latter.

SILVER POTASSIUM CYANIDE.

$AgK(CN)_2$.

Properties and Uses.—White crystals, soluble in water.

According to Behring this double cyanide has a powerful antiseptic action, while at the same time it is comparatively less poisonous to the organism attacked by the microbes. One part of the compound in 50,000 parts of blood serum formed a medium in which anthrax bacilli could not develop, while the fatal dose of the salt for guinea pigs amounted to $\frac{1}{3000}$ of the body weight.

SODIUM COMPOUNDS.

A number of newer sodium salts have been already described in the preceding section of the work. A few others of more or less importance are described here:—

Chloroborate.—A white, crystalline powder, readily soluble in water. This preparation is claimed to possess powerful antiseptic properties, that may be employed for the preservation of meat, as well as for medicinal purposes.

Gynocardate.—A yellowish-white powder, soluble in water, only partly in alcohol, a turbid mixture being produced.

Silico-fluoride, $(NaF)_2SiF_4$.—A white, crystalline powder, only difficultly soluble in water (about ½ per cent.). When moist, it has a strongly irritant action on the skin. Recommended under the name "Salufer" as an antiseptic by W. Thompson. A 2 per mille solution is non-irritant, and can be used for irrigating cavities. It is a powerful disinfectant for gynæcological purposes, and has been also useful as a styptic.

Tellurate, Na_2TeO_4.—A white powder, soluble in water.

Like the potassium salt, sodium tellurate is an excellent antihydrotic, the night-sweats of phthisis being unfailingly suppressed by it. In common with other tellurium compounds, it communicates a garlic-like odor to the breath, that may be only partially covered by peppermint.

Dose.—1 grain *pro die*.

Tetraborate. —Transparent, glassy masses, which very readily dissolve in cold water (*v.* Boric acid).

SOLANINE.

$C_{42}H_{57}NO_{15}$.

Nature and Source.—An alkaloidal glucoside obtained from parts of various solanaceous plants. Is also present in potato-sprouts.

Properties and Uses.—Acicular crystals, melting at 235° C.; very difficultly soluble in water, more readily so in hot alcohol. Is split up by dilute acids into dextrose and solanidin.

Solanine is not mydriatic. Has been used as an analgesic instead of morphine in neuralgia, the vomiting of pregnancy, in bronchitis, and asthma.

Dose.—⅙ to 1 grain, three times a day, in pill or powder; the hydrochloride has also been used subcutaneously in the same dose.

SOMATOSE.

Nature and Source.—A preparation of albumen in the form of readily absorbed albumoses.

Properties and Uses.—A slightly yellowish powder,

which is easily soluble in water and aqueous liquids. Odorless and almost tasteless. In distinction to most preparations of flesh for dietetic purposes it contains only small traces of peptone, whilst 90 per cent. of the dry substance consists of deutero- and hetero-albumose, the remainder consisting of the natural salts of fresh meat. The albumen in this form is considered readily assimilated by the system, and is free from the disadvantages of peptone.

Clinical experiments have demonstrated somatose to be an excellent dietetic, a complete substitute for albumen in the animal economy, well borne, and not productive of diarrhœa. Employed in carcinoma of the stomach, for phthisical patients with weak digestion, and in all forms of gastralgia and intestinal disorders.

Dose.—From ½ to 1 ounce in the course of the day, according to age and constitution of the patient, given in milk, cocoa, or soup.

SPARTEINE.

$C_{15}H_{26}N_2$.

Nature and Source.—An alkaloid obtained, with scoparine, from the tops and twigs of *Genista scoparia.*

Properties and Uses.—A volatile oily liquid, very unstable; boiling point 288° C. Only used in the form of salts, of which the most important is the

Sulphate.—Colorless, odorless, transparent crystals, readily soluble in water and alcohol; at 100° C. they lose 21.3 per cent. of water.

Properties similar to those of digitalis have been ascribed to sparteine, but some observers characterize its action as unreliable.

Other salts are the *hydrochloride* and *hydrobromide.*

Dose.—Of the sulphate, 1½ to 2 grains, repeated several times a day.

SPERMINE.

C_2H_5N.

Nature and Source.—A base obtained from the seminal fluid of various animals.

Properties and Uses.—A crystalline body, which absorbs water and carbonic acid from the air; readily soluble in water and absolute alcohol, insoluble in ether.

Spermine was specially recommended against nervous and cerebral depression, and has been used in senile and general debility, but further and more intimate study of its properties is still necessary and appears to be going on.

Various salts have been prepared, such as the hydrochloride and phosphate, but not much used.

Recently the application of this much discussed preparation has entered a new phase, and a new product prepared from bull testicles has appeared under the name of "*Suc testiculaire,*" either filtered by pressure of carbonic acid, or sterilized in the autoclave under pressure of carbonic acid. Recommended in a very heterogenous variety of diseases, in doses of 15 minims to 1½ drachms.

The employment of spermine therapeutically has been, moreover, the signal for the introduction of quite a number of new preparations, extracts from nearly every organ and gland in the body, of which the following may be mentioned.

Thyroid gland extract.—A glycerin or dilute alcoholic extract of the fresh thyroid gland, from which the active principle, which appears to be of enzymic nature, may be precipitated by calcium phosphate, and obtained in powder form. The preparation has gained quite an accepted position in the treatment of myxœdema, although occasional warnings of possible after-effects appear. Also employed in the treatment of psoriasis. A hypodermic injection of the glycerin extract, corresponding to about one-sixth of a gland, is given as a medium dose, once a day.

Cardine, an extract from the hearts of sheep, etc., prepared by digestion of the hacked flesh with an equal quantity of glycerin and of boric acid solution in a closed vessel for 8 to 12 months (!), and subsequent filtration. It is described as a clear yellowish liquid, 1 drachm of which injected subcutaneously into adults induces fuller pulse and increased arterial tension; recommended as a heart tonic and diuretic.

Nuclein, an extract of calf's milt, is a yellowish-white powder, soluble in alkaline fluids, which, according to Ger-

main Sée, may be given in doses of 30 to 45 grains per os, or in smaller doses subcutaneously, for the detection of latent tuberculosis.

Cerebrine and *Myeline*, preparations of the brain and spinal cord respectively, are reputed to rapidly restore nervous muscular and brain power.

STRONTIUM COMPOUNDS.

On the recommendation of French medical men, strontium salts have been administered in gastric affections, especially in hyperacidity, in Bright's disease, in epilepsy, and especially as substitutes for the corresponding calcium salts in renal disorders.

According to Papillon strontium may substitute calcium in bones, a statement disputed by Weiski, who maintains that whilst strontium is not a poison, animals fed with strontium instead of calcium compounds do not live, and that whilst strontium may be conveyed to the bones and tissues, it does not form an integral part of them. König, however, by experimenting with rabbits came to the same conclusion as Papillon.

Bromide, $SrBr_2,6Aq.$—Long, colorless needles, readily soluble in water.

Strontium bromide is better borne than other bromine salts, which only too often produce gastric disturbances, and has especially proved successful in epilepsy.

Dose.—30 to 60 grains *pro die*, dissolved in water; in epilepsy this daily quantity can be increased to 6½ drachms.

Iodide, $SrI_2,6Aq.$—Colorless, transparent needles, or in anhydrous form as a white granular powder. It turns yellow when exposed to light, owing to liberation of iodine.

Employed in 1 or 2 per cent. solution in scrofulous diseases.

Lactate, $Sr(C_3H_5O_3)_2,3Aq.$—A white, granular powder, which forms a clear solution in water.

Recommended in various kidney diseases, associated with albuminuria. Contra-indicated only in renal diseases with

reduced excretion of urine, or where uræmic symptoms appear. The lactate has also been employed by Laborde as a taenifuge with good results.

Dose.—Up to 2 drachms daily; ordinarily, however, it may be given in the same doses as the bromide.

Nitrate, $Sr(NO_3)_2$.—Colorless crystals, soluble in 5 parts of cold water.

Recommended in articular rheumatism especially.

Dose.—30 grains to 4 drachms.

Phosphate, $Sr_3(PO_4)_2$.—A white tasteless powder, sparingly soluble in water, but soluble in acids.

Considered by Laborde to be one of the most valuable nutritive and tonic medicaments known, and an excellent substitute for calcium phosphate.

Other salts of strontium employed are the *acetate*, as a taenifuge, the *sulphate* and *carbonate*.

STROPHANTHIN.

$C_{16}H_{26}O_8$.

Nature and Source.—A glucoside from the seeds of species of *Strophanthus*.

Properties and Uses.—A white, amorphous or crystalline powder, with an extraordinarily bitter taste; freely soluble in water and in alcohol.

Though in some cases inferior to digitalis as a cardiac, it is superior to it in the absence of any disturbing effect upon the respiratory centres. Its action on the vascular system is also less pronounced. The extensive literature of strophanthus contains the records of a very large number of cases in which it has done good service where other cardiacs have failed.

Dose.—$\frac{1}{60}$ to $\frac{1}{30}$ grain in water daily. Rarely hypodermically in doses of $\frac{1}{100}$ grain.

STRYCHNINE SALTS.

$C_{21}H_{22}N_2O_2.\overline{A}$.

The two principal newer combinations of strychnine are with saccharin and arsenicum.

The *Arseniate* is a white, micro-crystalline powder, with a bitter taste. Recommended, especially from America, as a tonic and diuretic, and in the treatment of phthisis.

Dose.—4 to 15 drops of a half per cent. solution (in liquid vaseline) daily.

TEREBENE.

$C_{12}H_{16}$.

Nature and Source.—A mixture of several terpenes, obtained by distilling oil of turpentine with sulphuric acid, and subsequently rectifying.

Properties and Uses.—A feebly yellow liquid, with a pleasant aromatic odor reminding of thyme, not very miscible with water, but somewhat more so with alcohol, and freely with ether. Is useful as an aerial disinfectant.

Internally terebene is used as an expectorant and for inhalation in chronic and recurrent bronchitis, and externally for dressing wounds (5 per cent. aqueous solution).

Dose.—4 to 6 or more drops every four hours, in emulsion or tablets.

TERPIN HYDRATE.

$C_{10}H_{18}(OH)_2$, Aq.

Nature and Source.—Prepared by the interaction of a mixture of rectified turpentine oil (4 parts), alcohol (of 80° T) (3 parts), and nitric acid (1 part), in shallow porcelain dishes during some days. A crystalline body separates, which is collected, drained, pressed between bibulous paper, and crystallized in the cold from 95 per cent. alcohol made alkaline with a little potash and soda. Terpin hydrate has been also obtained by treating various essential oils, such as eucalyptus oil, in a similar manner, from the terpenes contained in them.

Properties and Uses.—Terpin hydrate occurs in large, colorless and odorless, rhombic crystals, with a faint aromatic taste. Soluble in 250 parts of cold (15° C.) or 32 parts of boiling water, in 10 parts of alcohol, 100 of ether, 200 of chloroform, carbon bisulphide and benzene, but less in turpentine.

Melting point 116° to °117° C., with separation of the molecule of water. It has been included in the new United States Pharmacopœia.

A primary therapeutical effect of this compound is to increase the secretion of the bronchial mucous membrane; it is therefore indicated in chronic and subacute bronchitis, whooping cough, etc. In larger doses it stimulates renal activity, and hence is given in chronic nephritis. Its value is very probably dependent, to some extent, on its antiseptic properties.

Dose.—As an expectorant, 2 to 3 grains; in renal affections 5 to 6 grains, and in whooping cough 20 to 40 grains daily. Can be prescribed in pills, in tablets, and in mixture with spirit, syrup and peppermint water.

TERPINOL.

Nature and Source.—The product of boiling terpin, or terpin hydrate, with dilute mineral acids. Is not a simple body but a mixture of terpenes (terpinene, terpinolene and dipentene), with variable proportions of an alcohol, terpineol ($C_{10}H_{17}OH$).

Properties and Uses.—An oily body, with a hyacinthine odor; practically insoluble in water, but readily so in alcohol and ether; sp. gr. 0.852.

Terpinol has been used as a bronchial stimulant.

Dose.—8 to 15 grains, in capsules or pills.

Terpineol.—The alcohol referred to above is a thick, colorless, optically inactive liquid, with a pleasant hyacinthine odor, and a bitter, feebly pungent taste; s. g. 0.940 (at 15° C.).

It is recommended for the deodoration of iodoform.

THEOBROMINE.

$C_7H_8N_4O_2$.

Nature and Source.—An alkaloid obtained from the seeds of *Theobroma cacao*, Linné; a homologue of caffeine, containing a CH_2 group less than the latter.

Properties and Uses.—A white, crystalline powder, sparingly soluble in water, in alcohol and in ether.

Physiologically theobromine closely resembles caffeine, but is said to differ in having no irritating effect upon the nerve centres. Being insoluble it is unsuitable for use, and hence is employed in the form of a double salt (*v.* Diuretin).

THYMOL.

$C_{10}H_{13}HO$.

Nature and Source.—A phenolic stearoptene from the volatile oils of *Thymus vulgaris*, Linné, *Monada Punctata*, Linné, and *Carum ajowan*, Bent. and Hook.

Properties and Uses.—The physical and chemical properties of thymol are well known. Used as an antiseptic for the preservation of anatomical preparations and the embalming of corpses.

Internally in typhus, rheumatism, gastric fermentation, etc.; also as an antipyretic. Recommended for inhalation in pulmonary gangrene, bronchitis, whooping cough, and for mouth washes, against toothache, etc. In the treatment of wounds a 1 to 10 per mille solution is used; and in skin diseases, ointment and liniments (1 to 5 per cent.).

Dose.—1 to 2 grains in typhus, etc.; 8 to 15 grains as an antipyretic.

TUBERCULIN.

Nature and Source.—A sterilized glycerin extract of pure cultures of the tubercle bacillus, first prepared by Dr. Robert Koch.

Properties and Uses.—A transparent, yellowish liquid, stable in concentrated solution, but liable to change in the dilute solution.

Recommended as a diagnostic agent for the tuberculous diathesis, and as a remedy for the various forms of tuberculosis itself. A 1 per cent. solution is used (or 2 per mille for children) and a special syringe. The greatest care has to be taken in sterilizing the solution, the syringe, etc., and detailed instructions are given with each supply of the remedy. The literature of "Koch's treatment" has attained colossal dimensions, but perhaps definite judgment of its value must be still suspended.

Tuberculocidin, also called *Alexin* or *T. C.*, is a modification of tuberculin, introduced by Prof. Klebs as free from the sometimes injurious effects of tuberculin, which he ascribes to organic bases. The active substance of "Koch's lymph," according to Klebs, is an albumose, which does not produce the febrile symptoms of the crude substance. Tuberculocidin was put forward as a preparation of this pure albumose.

A number of new remedies prepared on similar principles have also appeared during the last two years, of which the following are the more important:

Antidiphtherine, prepared by Klebs from virulent cultures of diphtheria bacillus, in a manner analogous to tuberculin. The same precautions require to be adopted in its use as with the above preparations, and its therapeutical value is still in an unsettled state.

Cancroine.—In consequence of the toxic substance found by Adamkiewicz in the secretions of carcinoma parasites and used as a prophylatic against cancer, being analogous to *neurine* in physiological action and probably also in chemical composition, a solution of neurine in water, to which a little carbolic and citric acid is added, has been introduced under the name of "cancroine." Its action appears to be chiefly anodyne and deodorant, although said to have some specific effect.

Malleine, an extract of the cultures of the glanders bacillus, is used for the diagnosis of this disease. Horses suffering from glanders react after treatment with malleine by symptoms of fever.

VANILLIN.

$C_6H_3OH.OCH_3CHO.$

Nature and Source.—Occurs as a crystalline efflorescence on vanilla pods (*Vanilla planifolia*), also in many beet sugars, and in small quantities of the wood of many plants, where it probably originates in the oxidation of coniferin

$$COH—[CH(OH)]_4—CH_2—O—C_6H_3\begin{matrix}OCH_3\\C_3H_4(OH).\end{matrix}$$

Properties and Uses.—Acicular crystals, melting at 80° C., b. p. 285° C., subliming unchanged. Soluble in alcohol, ether and cloroform; less readily in water. Smells and tastes like vanilla.

Has been recommended as a stimulant in atonic dyspepsia.

VIEIRIN.

Nature and Source.—A bitter principle, from the bark of *Remijia vellozii*, a Rubiaceous plant found in Brazil.

Properties and Uses.—An amorphous, white substance, with an aromatic odor and bitter taste; m. p. 120° C. It is readily soluble in alcohol and in chloroform.

Esteemed in Brazil as a substitute for quinine in the treatment of fevers, and as a general tonic.

Dose.—1½ to 3 grains several times a day.

WRIGHTINE.

$C_{24}H_{40}N_2$.

Nature and Source.—An alkaloid from the barks of *Wrightia antidysenterica* and *Holarrhena antidysenterica.*

Properties and Uses.—Said to possess the properties of the drugs from which it is isolated, and hence recommended in diarrhœa and dysentery. Possibly it is also febrifuge and anthelmintic.

ZINC COMPOUNDS.

Borate, $ZnB_4O_7 + 7\,H_2O$.—An amorphous white powder, recently recommended by Kollo as a dusting powder for wounds.

Chrysophanate.—A brownish-red powder, that is readily taken up by water (made alkaline), and consequently is dissolved by the alkaline secretions of wounds.

Gynocardate.—A yellowish, granular powder, insoluble in water and diluted acids, readily soluble in ether, in alcohol and chloroform.

Recommended in the treatment of those forms of skin disease in which gynocardic acid has been used.

Permanganate.—In crystals, very similar to those of the potassium salt; very hygroscopic and readily soluble in water.

Used in the treatment of urethritis of all kinds, and in ophthalmic practice; is non-irritant in dilute solutions (1:4000). Alcohol, vegetable extracts and the like must not be ordered with it, as explosive mixtures are formed.

Sulphydrate, $Zn(SH)_2$ —A white precipitate, that must be kept under water, as it readily decomposes on keeping.

Used internally and externally with success in the treatment of chronic eczema, psoriasis and vegetoparasitic dermatoses. The ointment adopted was of the strength 10 per cent., with lanolin and lard (2 : 3).

Dose.—½ to 2 grains, several times a day, made up into pills with extract of gentian.

TABLES

OF

DOSES, SOLUBILITY, MELTING and BOILING POINTS of NEW REMEDIES.

Prof. Demme, of the Jenner Children's Hospital, Berne, gives the following:—

Dosage of Antipyretics for Children.

	Children of		
	2—4 years.	5—10 years.	11—15 years.
Acetanilide, 1—3 times daily, pro dosi	1—1½ grains	2— 4 grains	4— 5 grains
Antipyrine, 2—3 times daily, pro dosi	3—6 grains	8—10 grains	12—15 grains
Phenacetine, single dose.	2—4 grains	4— 5 grains	8 grains
Quinine salts, single dose	3—6 grains	8—10 grains	10—15 grains
Salol, 3—4 times daily, pro dosi	4—6 grains	8—12 grains	12—15 grains
Thalline sulphate, every 2 hours	⅙ grain	⅓ grain	½— 1 grain

Table I.

Average Doses of New Remedies.

	Pro dosi.	Pro die.
Acetanilide	3— 8 grains	45 grains
Agathin	8 "	24 "
Alphol	8—15 "	
Amylene hydrate	45—60 "	2 drms.
Analgene	8 "	40 grains
Antipyrine	15—30 "	
Antispasmin	⅛— 1½ "	

TABLE I.—(*Continued.*)

	Pro dosi.	Pro die.
Benzanilide	15—45 grains	
Benzosol	4—12 "	12—36 grains
Betol	5— 8 "	15—30 "
Bromacetanilide	2— 8 "	
Bromamide	10 "	
Bromoform	1— 2 minims	5—20 minims
Bromol	1 grain	8 grains
Caffeine-chloral	3— 5 grains	
Caffeine tri-iodide	2— 4 "	
Chinoline salts	5—20 "	
Chloralamid	30—45 "	1½ drms.
Chloralammonium	30—45 "	1½ "
Chloralose	1½ "	
Chloralurethane	10—40 "	
Creolin	5 minims	
Creosote	3 "	
Creosote carbonate	15 "	
Dermatol	8 grains	24 grains
Dithiosalicylic acid II	8 "	30 "
Diuretin	15 "	45—90 "
Ethoxy-caffeine	3 "	
Ethyl bromide	5—10 drops	
Euphorin	6— 8 grains	20—30 "
Exalgine	½— 4 "	
Formanilide	2— 4 "	8 "
Gallobromol	30—45 "	
Guaiacol	2 minims	15 minims
Guaiacol carbonate	6— 8 grains	1½ drms.
Guaiacol salicylate	15 "	
Hydracetine	⅙— 1 "	2 grains
Hydroquinone	3— 8 "	
Hypnal	15—30 "	
Hypnone	3— 8 minims	
Ichthyol	4—20 "	
Iodol	3 grains	8—15 "
Iodopyrine	8—24 "	
Lactophenine	1— 1½ "	
Malakin	15 "	60—90 "
Methacetine	5—15 "	
Methylal	15—30 minims	2 drms.
Methylene blue	1½— 8 grains	

TABLE I.—(*Continued.*)

	Pro dosi.	Pro die.
Naphtalene	1— 2 grains	8 grains
Neurodin	15 "	
Oleocreosote	45—90 minims	
Orexine hydrochloride	5— 8 grains	
Paraformic aldehyde	8–15 "	
Paraldehyde	½— 1 drm.	
Pental (by inhalation)	2— 3 drms.	
Phenacetine	8—12 grains	1½ drms.
Phenocoll hydrochloride	8—15 "	1½ "
Piperazine	15 "	45 grains
Resorcin	3— 8 "	45 "
Salacetol	30—45 "	
Salicylamide	3— 5 "	15 "
Salipyrin	15 "	
Salocoll	15 "	
Salol	15—30 "	2 drms.
Salophen	15—30 "	
Sodio theobrom.salicyl.(*v.*Diuretin)		
Sodium ichthyolsulphonate	3 "	10 grains
" paracresotate	15—30 "	
Somnal	30 minims	
Sulphonal	15—30 grains	1½ drms.
Symphorol	15 "	60 grains
Tetronal	15—30 "	1½ "
Thalline salts	2— 5 "	
Thermodin	8–10 "	25—30 "
Thioform	5 "	15 "
Thiol, liquid	4—20 minims	
" powdered	2—10 grains	
Thymacetin	5—15 "	
Tribromophenol (*v.* Bromol)		
Trional	15—30 "	1½ drms.
Urethane	15—40 "	
Uropherin	15 "	45 grains

TABLE II.

Solubility of New Remedies

in Water and Spirit.

	1 part dissolves in		Remarks.
	Water (15°)	Spirit (15°)	
Acetanilide	200	10	In about 18 parts of boiling water, 40 of glycerin. Ph. G. 194 of water, and 3½ of alcohol.
Agathin	insoluble	soluble	
Alphol	insoluble	soluble	
Alumnol	soluble	slightly sol.	Generally used in 1 to 2 per cent. solution.
Amylene hydrate	8	freely sol.	Saturated aqueous solutions become turbid when warmed.
Analgene	insoluble	slightly sol.	Soluble in hot alcohol.
Anthrarobin	insoluble	5	Dissolves in aqueous alkalies, also in glycerin.
Antipyrine	1	1	
" " benzoate	slightly sol.	freely sol.	Also taken up by ether.
Antispasmin	soluble	insoluble	Aqueous solution alkaline, precipitated by weak acids.
Apyonin	little soluble	freely sol.	
Aristol	insoluble	slightly sol.	Taken up by trituration with fatty oils.
Asaprol	1½	3	
Benzanilide	insoluble	60	
Benzonaphtol	insoluble	soluble	
Benzophenoneid	100		
Benzosol	insoluble	soluble	Readily soluble in hot alcohol.
Betol	insoluble	diffic. sol.	In about 3 of boiling alcohol.
Bromacetanilide	insoluble	diffic. sol.	
Bromamide	insoluble	slightly sol.	
Bromoform	300	freely sol.	
Bromol	pract. insol.	freely sol.	Also soluble in ether, chloroform, glycerin and oils.
Caffeine-chloral	freely sol.		
Caffeine-triiodide	insoluble	soluble	
Chinoline	pract. insol.	5	
" " salicylate	80	freely sol.	
" " tartrate	80	150	
Chloralamid	10	2—3	Is only slowly taken up by water; must not be heated.

TABLE II.—(*Continued.*)

	1 part dissolves in		Remarks.
	Water (15°)	Spirit (15°)	
Chloralammonium . . .			Chloralammonium decomposes even in the cold.
Chloralose	170	soluble	
Chloral-urethane	insoluble	soluble	Decomposes when heated in solution like all these chloral compounds.
Creolin		soluble	Forms emulsion with water.
Creosote	pract. insol.	freely sol.	Dissolves in 120 parts of hot water.
" " carbonate . . .	insoluble	freely sol.	
Cresalols	insoluble	readily sol.	Also taken up by oils.
Cresol, ortha-	37	readily sol.	
" meta-	200	readily sol.	
" para-	50	readily sol.	
Cresol iodide	insoluble	readily sol.	Taken up by fatty oils.
Cresotic acids	diffic. sol.	readily sol.	
Dermatol	insoluble	insoluble	
Diaphterin	soluble	soluble	Usually employed in 1 to 2 per cent. aqueous solution.
Diaphtol	slightly sol.	soluble	Soluble in 35 pts. boiling water.
Di-iodoform	insoluble	slightly sol.	
Di-iodo-β-naphtol	insoluble	sparingly	Abundantly taken up by chloroform.
Dithiosalicylic acid I	insoluble	insoluble	
" " " II.	insoluble	readily sol.	
Diuretin	freely sol.		Precipitated by weak acids.
Dulcin	800	25	
Ethoxycaffeine	slightly sol.	readily sol.	
Ethyl bromide	insoluble	soluble	Also miscible with ether, chloroform and oils.
Ethylene bromide	insoluble	freely misc.	
Euphorin	insoluble	readily sol.	Taken up by mixtures of alcohol and water (wines).
Europhen	insoluble	readily sol.	Also taken up by fatty oils.
Exalgine	diffic. sol.	readily sol.	
Formanilide	soluble	readily sol.	
Formicaldehyde	in all propor.	in all propor	
Fluorescin	soluble		

TABLE II.—(*Continued.*)

	1 part dissolves in		Remarks.
	Water (15°)	Spirit (15°)	
Gallacetophenone	about 500	readily sol.	Readily soluble in hot water, and a 4 per cent. solution may be made in 30 per cent. sod. acetate.
Gallanol	nearly insol.	soluble	Soluble in hot water.
Gallobromol.....	12	soluble	In 2 to 4 per cent. aqueous solution.
Guaiacol	85	readily sol.	
" " crystalline ..	50	readily sol.	
" " carbonate...	insoluble	slightly sol.	Dissolved and decomposed by alkalies.
" " salicylate ...	insoluble	slightly sol.	Dissolved and decomposed by alkalies.
Hydracetine.....	50	readily sol.	Taken up by 8 to 10 of boiling water.
Hydronaphtol	little soluble	soluble	
Hydroquinone	diffic. sol.	readily sol.	Also readily in hot water.
Hydroxylamine hydr..	1	15	Also in glycerin.
Hynal.....	5—6		
Hypnone	insoluble	readily sol.	Also miscible with fatty oils.
Ichthyol.....	freely sol.	partly sol.	
Iodantipyrine	diffic. sol.	diffic. sol.	More freely soluble in the hot menstrua.
Iodol.....	prac. insol.	3	Alcohol solutions are precipitated by water, but not by glycerin.
Iodophenine.....		soluble	Evolves iodine when merely mixed with water.
Kairin	6	20	
Lactophenine	soluble	readily sol.	
Lanolin	insoluble	80 (78°C.)	Readily miscible with an equal weight of water.
Loretin.....	500	soluble	Readily soluble in alkalies.
Losophan	slightly sol.	readily sol.	Employed in 1 to 2 per cent. aqueous solution.
Lycetol	freely sol.		
Lysol	freely sol.	freely sol.	
Malakin.....	prac. insol.	diffic. sol.	Easily soluble in hot alcohol.
Mercury sozoiodol	500		More soluble in solution of common salt.
Metaldehyde	insoluble	readily sol.	

TABLE II.—(*Continued.*)

	1 part dissolves in		Remarks.
	Water (15°)	Spirit (15°)	
Methacetine	530	readily sol.	Also taken up by glycerin.
Methylal	3	readily sol.	Miscible with oils.
Methyl chloride			Water absorbs 4 and alcohol 35 volumes.
Methylene blue	slight. sol.	readily sol.	
" " chloride	slight. sol.	readily sol.	
Microcidin	3		
Monobromphenol	slight. sol.	readily sol.	
Monochlorphenol	slight. sol.	readily sol.	
Naphtalene	insoluble	diffic. sol.	Readily soluble in hot alcohol; also taken up by fatty and essential oils.
Naphtol	1000	readily	Solubility in water increased by the presence of boric acid.
Neurodin	slightly sol.		
Oleocreosote	insoluble	fairly sol.	Mixes easily with oils.
Orexine hydrochlor.	freely sol.	freely sol.	
α-Oxynaphtoic acid	prac. insol.	10	Somewhat soluble in hot water.
Paraformic aldehyde	soluble	soluble	
Paraldehyde	10	readily sol.	A solution saturated at 15° separates paraldehyde when heated. Ph. G. 8½ parts of water.
Pental	insoluble	freely sol.	
Phenacetine	prac. insol.	diffic. sol.	Ph. G. 1,400 parts of water and 16 parts of alcohol.
Phenocoll acetate	3½		
" " carbonate	insoluble		Readily dissolved by weak acids.
" " hydrochl.	16		
" " salicyl	soluble		
Piperazine	very sol.		
Potass. sozoiodol	50		
Pyoktanin, blue (Methyl-violet)	50 (?)		Generally used in 1 per cent. solutions and upwards.
Pyridine		1	Miscible with water in all proportions.
Pyrocatechin	soluble	soluble	
Resopyrin	insoluble	5	
Resorcin	2	readily sol.	Ph. G. 1 in 1 of water, and 2 in 1 of alcohol.
Saccharin	400	30	

TABLE II.—(*Continued.*)

	1 part dissolves in		Remarks.
	Water (15°)	Spirit (15°)	
Salacetol	insoluble	15	Soluble in 25 to 30 pts. of fatty oils, and also in dilute alkalies.
Salicylamide	250	soluble	
Salipyrin	diffic. sol.	readily sol.	
Salocoll	200	readily sol.	
Salol	insoluble	10	Alcoholic solutions form emulsions with water.
Salophen	insoluble	freely sol.	
Sodium paracresot			Soluble in about 24 pts. of warm water.
" " sozoiodol	14		
Sozal	freely sol.	slightly sol.	Used in about 1 per cent. aqueous solution.
Sozoiodol	readily sol.	readily sol.	Also taken up by glycerin.
Sulphaminol	insoluble	soluble	
Sulphonal	450	65	B. B. Add.: "in about 50 fl. parts of cold rectified spirit."
Sulphosalicylic acid	readily sol.	readily sol.	
Symphorol L	readily sol.	nearly insol.	
" " N	50	nearly insol.	
" " S	readily sol.	nearly insol.	
Tetronal	450	readily sol.	
Thalline sulphate	7	100	2 to 1 of boiling water.
" " tartrate	10	slightly sol.	
Thermodin	soluble		
Thioform	insoluble	insoluble	Gradually dissolved out by alkalies.
Thiol	soluble	soluble	
Thiophen	insoluble		
Thioresorcin		diffic. sol.	
Thiosinamine	slightly sol.	readily sol.	Employed in 15 to 20 per cent. dilute alcoholic solution.
Thiuret	350	insoluble	
Thymacetin	diffic. sol.		
Trional	320	readily sol.	
Urethane	1	0.6	
Uropherin	soluble		Aqueous solution strongly alkaline, precipitated by weak acids.
Zinc sozoiodol	20	soluble	

TABLE III.

Melting and Boiling Points of New Remedies,

in Centigrade degrees.

	M. p.	B. p.	Sp. gr. and Remarks.
Acetanilide	114°	295°	B. P. Add.: m. p. = 112.8° C.
Agathin	74°		
Analgene	208°		
Amylene hydrate	—12°	102.5°	S. g. 0.81.
Antipyrine	113°		B. P. Add: m. p. = 110° C.
Asaprol	192°		
Benzanilide	163°		
Benzonaphtol	110°		
Benzosol	50°		
Betol	95°		
Bromacetanilide	165°		
Bromamide	117°		
Bromoform	4.5°	149°–150°	S. g. 2.9.
Bromol	95°		
Chinoline		237°	S. g. 1.084.
Chloralamid	115°		
Chloral-ammonium	62°–64°		
" -urethane	100°–103°		
Chloralose	184°–186°		
Cresalol, ortho-	35°		
" meta-	74°		
" para-	39°		
Cresol, ortho-	31°	188°	S. g. 1.05 at 20° C.
" meta-		201°	S. g. 1.028 at 20° C.
" para-	36°	198°	S. g. 1.038 at 20° C.
Cresotic acid, ortho-	160°		
" " meta-	177°		
" " parr-	151°		
Diaphterin	85°		
Ethoxycaffeine	138°–139°		
Ethyl bromide		38°–39°	S. g. 1.38—1.39.
" chloride		10°	Very inflammable.
Ethylene bromide		191°	S. g. 2.163.
Euphorin	51°		
Europhen	110°		"Sinters" at 70° C.
Exalgine	100°	240°–250°	

TABLE III.—*Continued.*

	M. p.	B. p.	Sp. gr. and Remarks.
Formanilide	46°		
Formic aldehyde		—21°	
Gallanol	205°		
Guaiacol	33°	205°	S. g. 1.117.
" carbonate	78°–84°		
" salicylate	65°		
Hydracetine	128°–129°		
Hydroquinone	172.5°		When rapidly heated it decomposes.
Hypnal	67°–68°		
Hypnone	20.5°	210°	S. g. 1.032.
Iodantipyrine	160°		
Iodophenine	130°–131°		
Iodol			Decomposes between 140° and 150°.
Lanolin	40°–44°		P. B. Add: 37.8° and 44.4°.
Loretin	280°		
Losophan	121°		
Lycetol	118°		Volatilizes at high temperatures.
Malakin	92°		
Metal ehyde			Sublimes without melting at 112—115°, being partly decomposed.
Methacetine	127°		Distils unchanged.
Methylal		42°	S. g. 0.855.
Methyl chloride		21°	S. g. 0.9915 (at —23.7°)
Methylene chloride		41°–42°	S. g. 1.354.
Monobromphenol		194°	
Monochlorphenol	37°		
Naphtalene	80°	218°	
Naphtol	123°	286°	
Neurodin	87°		
α-Oxynaphtoic acid	185°		Decomposes as it melts
Paraformic aldehyde	171°		Volatilizes at high temperatures.
Paraldehyde	10°	124°	S. g. 0.998.
Pental		38°	Is highly inflammable.
Phenacetine	135°		

TABLE III.—*Continued.*

	M. p.	B. p.	S. g. and Remarks.
Phenocoll	115°		
Piperazine	104°	145°	
Pyridine		117°	S. g. 0.9858 (0° C.)
Pyrocatechin	104°	240°–245°	
Resopyrine			"Melts very readily."
Resorcin	118°	276°	Ph. G.: melts at 100° to 111°.
Saccharin	200°		Decomposes and partly volatilizes when heated.
Salacetol	71°		
Salicylamide	142°		
Salipyrine	91.5°		
Salol	42°–43°		
Salophen	187°–188°		
Sulphaldehyde	—2°		
Sulphaminol	155°		
Sulphonal	125°–126°		B. B. Add. 125°.5.
Tetronal	85°		
Thalline sulphate	100°+		Decomposes above the melting point.
Thermodine	86°–88°		
Thiosinamine	74°		
Thiuret	215°		
Thiophene		84°	
Trional	76°		
Urethane	47°–50°	170°–180°	Scarcely decomposes even when boiled.

TABLE IV.—Detection of New Remedies in Urine (according to Braeutigam).

Name.	Color.	Alkaline Reagents.	Acid Reagents.	Spectrum Analysis. Polarisation.	Special Reagents.	Oxidizing and Reducing Agents.	Extractives.	Remarks.
Acetanilide	.....	.....	10 cc. boiled with 2 cc. hydrochloric acid, 2 cc. 3 per cent. carbolic acid and a few drops of lime solution added when cold, gives a red color changing to blue with excess of ammonia.	Rotates to left owing to the presence of a glycuronic acid compound.	.....	Reduces Fehling's solution	.....	Occurs in urine as esters of ethyl-sulphuric and of glycuronic acids, which after boiling with acids give the usual indophenol reaction.
Analgene.....	Blood-red after large doses or continued use.	Blood-red color changed to yellow (Distinction from blood).	Color intensified by small quantities, destroyed by larger quantities.	.....	Boiled with ferrichloride brownish-red.	.....	The alkaline urine shaken with ether yields a residue giving the characteristic tests for ethoxyamidochinoline (q. v.)	Disintegrated in the organism into benzoic acid and ethoxyamidochinoline.
Antipyrine	Darker than normal.	.....	.....	.....	Purple-red with ferric chloride, unchanged on boiling, destroyed by acids.	.....	Ether extracts from the acidified urine a substance which is colored brown by ferric chloride.	Eliminated from system partly unaltered. Changes undergone by remainder not understood.

Name.	Color.	Alkaline Reagents.	Acid Reagents.	Spectrum Analysis. Polarisation.	Special Reagents.	Oxidizing and Reducing Agents.	Extractives.	Remarks.
Atropine								Urine treated with alcohol and tartaric acid, filtered, filtrate evaporated, extracted with ether, then made alkaline and again extracted with ether. The second ethereal residue evaporated with a few drops of nitric acid. Violet and than cherry-red color on addition of alcoholic potash to the residue.
Arbutin (Bear berry)	Darker than normal. On standing olive-green from surface downwards owing to presence of hydroquinone			Rotates to the left.		Does not reduce Fehling's.	Ether dissolves out hydroquinone.	Free hydroquinone and its ethyl-sulphuric acid ester occurs as well as unaltered arbutin.
Benzoic Acid								Converted into hippuric acid, which is extracted from the evaporated urine by ether and recognized by nitrobenzene odor on heating with nitric acid.
Carbolic Acid	On standing dark-green to blackish, from formation of hydroquinone.				On addition of acetic acid and barium chloride no precipitate, but first on warming with hydrochloric acid.		On acidification and destillation, bromine water produces a yellowish precipitate (tribromophenol).	Carbolic acid occurs as phenyl - ethyl - sulphuric acid, which is not decomposed by acetic acid, but only by hydrochloric acid. Tar, creosote, guaiacol, resorcin, and other benzene derivatives yield similar reactions.

Name.	Color.	Alkaline Reagents.	Acid Reagents.	Spectrum Analysis. Polarisation.	Special Reagents.	Oxidizing and Reducing Agents.	Extractives.	Remarks.
Chloral hydrate	.....	.....	.....	Rotates to the left (Urochloralic acid).	Urine decolorized with acetate of lead, made alkaline and filtered, gives a red coloration on boiling with a little resorcin.	Reduces Fehling's solution	.....	Occurs mostly as urochloralic acid.
Chloroform	.....	Potash and thymol give a dark blue color on warming. Alcoholic potash and aniline the isonitrile odor.	.....	.....	As chloral hydrate.	Reduces Fehling's solution	.....	Occurs in urine unaltered. Urine of high specific gravity and frequently containing albumen and sugar.
Chrysophanic Acid. (Senna) (Rhubarb)	Yellow or greenish-yellow.	Red.	Destroys the red color given by alkalies.	No characteristic absorption.	Baryta and lime water produce red precipitates.	Destruction of red color with sodium amalgam.	Ether extracts yellow coloring matter.	.....
Copaiba	.....	.....	Rose color, on warming violet.	Rotates to left.	.....	Reduces Fehling's solution	"Copaiba-red" extracted by chloroform.	The nitric acid test for albumen fails after copaiba or sandalwood administration.
Guaiacol, *vide* Carbolic acid.								
Hypnone	.....	.....	.....	.....	.....	.....	.....	As for benzoic acid. Hypnone is oxidized in the organism to benzoic and carbonic acids.

Name.	Color.	Alkaline Reagents.	Acid Reagents.	Spectrum Analysis. Polarisation.	Special Reagents.	Oxidizing and Reducing Agents.	Extractives.	Remarks.
Morphine	.....	.....	.....	.....	.....	Reduces Fehling's solution	.....	Urine treated as for atropine (q. v.) but finally extracted with amyl alcohol. The extract gives a blue color with ferric chloride or with Fröhde's reagent.
Naphtalene	Dark yellow to brown.	Slight browning with blue fluorescence.	Hydrochloric and nitric acids a momentary red color. Strong sulphuric dark-green.	.....	Filter paper dipped in urine turns red on touching with diazoamido-benzene and warming.	Citron-yellow color with chloride of lime solution.	Ethereal extract with 1 per cent. resorcin solution and a few drops ammonia, gives a blue-green color.	Naphtalene appears to be eliminated as Beta-naphtol or as Beta naphtol glycuronic acid.
Nicotine	.....	.....	.....	.....	.....	.....	.....	As for atropine (q.v.) Ethereal residue a yellow or brown oily mass which on addition of an ethereal iodine solution separates ruby red crystals on standing.
Phenacetine ...	.....	.....	.....	.....	Burgundy red with ferric chloride.	Reduc'g substance (not sugar) present.	.....	Occurs as amidophenol or amidophenetol (*vide* Acetanilide).
Phenocoll	Brownish red to deep brown.	.....	.....	.....	Darkens with ferric chloride, but lightens on further addition of sulphuric acid assuming a peculiar tone.	.....	.....	Eliminated apparently very rapidly, as the ferric chloride reaction fails after 12 hours.

Name.	Color.	Alkaline Reagents.	Acid Reagents.	Spectrum Analysis Polarisation.	Special Reagents.	Oxidizing and Reducing Agents.	Extractives.	Remarks.
Piperazine . .	.....	.....	.....	... .	Potassium bismuth iodide produces characteristic red crystalline precipitate in acidified and filtered urine.	.....	. .....	Passes the system almost completely undecomposed.
Quinine	Frequently darker than normal.	.....	.....	.....	Shaken with ammonia and ether, the residue dissolved in dilute acid gives an emerald green with chlorine water and ammonia	.....	.....	.....
Resorcin, *vide* Carbolic acid.								
Rhamnoxanthin (Cascara Sagrada)	Yellow or reddish-yellow.	Red color and precipitate on boiling.	Destruction of red color.	The alkaline urine darkens the right side of spectrum.	Baryta and lime water produce a red precipitate.	Sodium amalgam destroys the red color.	Ether extracts a yellow coloring matter.	.....
Salicylic Acid ..	.....	.....	.....	Rotates to the left.	Violet with ferric chloride. Emerald green with copper sulphate.	Reduces Fehling's slightly.	.....	Converted into salicyluric acid in the organism.
Salipyrin	.....	.....	.....	.....	With ferric chloride deep violet, subsequently deep red.	.....	.....	.....

Name.	Color.	Alkaline Reagents.	Acid Reagents.	Spectrum Analysis. Polarisation.	Special Reagents.	Oxidizing and Reducing Agents.	Extractives.	Remarks.
Salol	Dark-green to greenish-black on standing.	.....	.....	Rotates to the left.	Red with ferric chloride. Same behavior towards acetic acid and barium chloride as carbolic acid.	Reduces Fehling's solution	.....	Occurs as phenyl-ethyl sulphuric acid and salicyluric acid.
Santonin	More yellow than normal.	Red.	Decolorized.	Alkaline urine darkens right side of spectrum.	Baryta and lime water produce a colorless precipitate, the urine remaining red.	No effect.	.....	Red color disappears after 24 to 48 hours.
Strychnine	.....	.....	.....	.....	.....	.....	.....	Extracted from urine as atropine, the ethereal residue gives a temporary blue to violet coloration with bichromate of potassium and sulphuric acid.
Sulphonal	Sometimes dark-red (hæmatoporphyrin)	.....	.....	In hydrochloric acid exhibits two absorption lines, one thin in the yellow and one broad in the green; in alkaline solution four lines, two in orange, one in yellow and one in green.	Red coloring matter precipitated by alkaline barium chloride solution.	.....	.....	Converted into readily soluble organic sulphur compounds. Frequently odor of fresh fruit.

NAME.	COLOR.	ALKALINE REAGENTS.	ACID REAGENTS.	SPECTRUM ANALYSIS. POLARISATION.	SPECIAL REAGENTS.	OXIDIZING AND REDUCING AGENTS.	EXTRACTIVES.	REMARKS.
Tannic Acid ...	.....	.....	.....	.....	Blue-black with ferric chloride.	.....	.....	Converted into gallic acid.
TerpeneHydrate	Darker than normal.	.....	.....	.....	Evaporated residue of urine taken up with alcohol gives a red color on warming with antimonious chloride.	.....	.....	.....
Thallin	Yellow to dark-brown with green tinge.	.....	.....	.....	Purple-red with ferric chloride.	.....	Ether extracts a substance colored green by ferric chloride.	Eliminated partly unchanged, partly as esters.
Tolypyrine	Same reactions as for		Antipyrine.	.....	.....	.....	....	.....
Turpentine Oil	Darker than normal.	.....	On boiling a precipitate soluble in alcohol.	.....	.....	.....	.....	Pleasant violet odor.
Urethane.....	Normal.	.....	.....	.....	Mercuric chloride added to a solution of the ethereal extract, gives a yellowish-white precipitate.	Reduces slightly.	Ether dissolves out urethane.	.....

TABLE V.

Commercial Names of New Remedies.

Commercial Name.	Chemical Composition, or Description.
ABRASTOL	A sulphonated derivative of β-naphtol.
AGATHIN	Salicyl-alpha-methylphenylhydrazone.
AGOPYRIN	Mixture of salicin, ammonium chloride and cinchonine sulphate.
ALEXINE T. C.	Tuberculocidin.
ALPHOL	Salicylic acid α-naphtol ester.
ALUMNOL	Aluminium salt of β-naphtoldisulphonic acid.
AMIDOL	Di-amido-phenol hydrochloride.
ANALGENE	Ortho-ethoxy-ana-monobenzoyl-amidochinoline.
ANALGESINE	Antipyrine.
ANALGINE	Mixture of acetanilide, bicarb. soda, etc.
ANGIONEUROSIN	Nitroglycerine.
ANNIDALIN	Dithymol di-iodide.
ANTIBACTERIN	Mixture of crude aluminium sulphate and soot.
ANTICHOLERIN	From cholera cultivations.
ANTIDIPHTHERIN	From diphtheria cultivations.
ANTIFEBRIN	Acetanilide.
ANTIFUNGIN	Magnesium borate.
ANTIKAMNIA	Mixture of acetanilide, sodium carbonate and caffeine.
ANTIKOL	Mixture of acetanilide, sodium bicarbonate and tartaric acid.
ANTINERVINE	Mixture of acetanilide, ammonium bromide and salicylic acid.
ANTINONNIN	Orthodinitrocresolate of potassium, with soap and glycerin.
ANTIPYRINE	Phenyl-dimethyl-pyrazolon.
ANTIRHEUMATINE	Mixture of sodium salicylate and methylene blue.
ANTISEPSIN	Monobrom-acetanilide.
"	Serum of animals treated with iodine trichloride.
ANTISEPTIN.	Mixture of zinc iodide, zinc sulphate, boric acid and thymol.
ANTISEPTOL	Iodosulphate of cinchonine.
ANTISPASMIN	Narcein-sodium—sodium salicylate.
ANTITHERMINE	Phenylhydrazin-lævulinic acid.
ANTITOXINE	General name for bacterial products.
APYONIN	Substitute for yellow pyoctanin (in France).
ARISTOL	Dithymoldiiodide.
ASAPROL	Calcium salt of β-naphtol α-monosulphonic acid

TABLE V.—*Continued.*

Commercial Name.	Chemical Composition, or Description.
ASBOLIN	Alcoholic tar distillate.
ASEPTIC ACID	Mixture of hydrogen peroxide solution with boric and salicylic acids.
ASEPTOL	Phenolsulphonic acid.
BENZONAPHTOL	β-naphtol benzoate.
BENZOPARACRESOL	Paracresol benzoate.
BENZOSOL	Guaiacol benzoate.
BERGAMIOL	Linalool acetate.
BETOL	β-naphtol salicylate.
BOROL	Mixture of boric acid and acid sodium sulphate.
BROMAMIDE	Bromaniline hydrobromide.
BROMOL	Tribromophenol.
CAFFEORESORCIN	Compound of caffeine and resorcin.
CAMPHAR	Solution of camphor in 50 per cent. alcohol.
CAMPHOID	Solution of camphor and collodion in absolute alcohol.
CANCROIN	A solution of neurine with citric and carbolic acids.
CARDIN	Extract from bullock's heart.
CEREBRIN	Extract of brain matter.
CHELEN, OR KELENE	Ethyl-chloride.
CHLORALAMID	Chloral-formamide.
CHLORALOSE	Condensation product of glucose and chloral.
CHLOROBROM	Solution of potassium bromide and chloralamid.
CHLOROL	Corrosive sublimate solution containing copper sulphate.
CHLORYL	Mixture of ethyl and methyl chlorides.
CREOLIN	Coal-tar preparation.
CREOSOTAL	Creosote carbonate.
CRYSTALLIN	Solution of collodion in methyl alcohol.
DERMATOL	Basic bismuth gallate.
DEXTROCOCAINE	Isomeride of Cocaine.
DEXTROSACCHARINE	Mixture of glucose and saccharine.
DIABETIN	Lævulose.
DIAPHTERIN	Oxychinaseptol, a combination of two molecules oxychinoline with one molecule of phenol-sulphonic acids.
DI-IODOFORM	Tetra-iodo-ethylene.
DISINFECTIN	Mixture of crude naphta and sulphuric acid.
DITHION	Mixture of sodium salts of isomeric dithiosalicylic acids.
DIURETIN	Theobromine sodium—sodium salicylate.

TABLE V.—*Continued.*

Commercial Name.	Chemical Composition, or Description.
DULCIN	Paraphenetolcarbamide.
EMOL	A kind of soapstone.
EPIDERMIN	An ointment base, consisting of white wax, water and gum.
EUCALYPTO-RESORCIN	Compound of eucalyptol and resorcin.
EULYPTOL	Mixture of salicylic acid, carbolic acid and eucalytus oil.
EUPHORIN	Phenylurethane.
EUROPHEN	Isobutyl-ortho-cresol iodide.
EXALGINE	Methylacetanilide.
EXODYNE	Mixture of acetanilide, sodium salicylate and sodium bicarbonate.
FERRATIN	Iron albuminate preparation.
FORMALIN, FORMOL	Formic aldehyde, (40 per cent. aqueous solution).
FORMALITH	Kieselguhr, saturated with formalin.
FOSSILIN	Vaseline.
GALLACETOPHENONE	Methylketotrioxybenzene.
GALLAL	Aluminium gallate.
GALLANOL	Gallic acid anilide.
GALLOBROMOL	Dibromo-gallic acid.
GELATOL	An ointment base containing oil, glycerin, gelatine and water.
GLACIALIN	Mixture of borax, boric acid and sugar.
GLONOIN	Nitroglycerin.
GLUSIDE	Saccharin.
HÆMOGALLOL	Product of action of pyrogallol on the coloring matter of blood.
HÆMOL	Product of action of zinc-dust on the coloring matter of blood.
HYDRACETINE	Acetylphenylhydrazine.
HYPNAL	Chloral-antipyrine.
HYPNONE	Acetophenone.
IATROL	Oxy-iodo-ethylaniline (?).
ICHTHYOL	Ammonium salt of ichthyol-sulphonic acid.
INGLUVIN	The pepsin of fowl's crops.
IODOCAFFEINE	Mixture of caffeine with sodium iodide.
IODOL	Tetra-iodo-pyrrol.
IODOLIN	Chinoline-chloro-methylate chlor-iodolate.
IODOPHENINE	Iodo-phenacetin (Tri-iodo-diphenacetin).
IODOPYRINE	Mono-iodo-antipyrine.

TABLE V.—*Continued.*

Commercial Name.	Chemical Composition, or Description.
Iodotheine	Mixture of caffeine with sodium iodide.
Iodotheobromine	Mixture of theobromine with sodium iodide.
Izal	Coal-tar preparation.
Katharin	Carbon tetrachloride.
Kelene, or Chelen	Ethyl chloride.
Lactophenin	Lactyl-phenetidine.
Lanoline	Purified wool-fat emulsified with water.
Lipanin	Olive oil, containing about 6 per cent. free oleic acid.
Losophan	Tri-iodo-metacresol.
Loretin	Iodo-oxychinoline-sulphonic acid.
Lysol	A cresol preparation.
Malakin	Salicylic aldehyde-para-phenetidine.
Methacetine	Para-acetyl anisidin.
Methonal	Dimethyl-sulphone-dimethyl-methane.
Methylal	Methylene dimethyl ether.
Metol	Mono-methyl-paramido-meta-cresol hydrochlor-[ide.
Methozine	Antipyrine.
Microcidin	β-naphtol-sodium.
Migranin	Mixture of antipyrine, caffeine and citric acid.
Mollin	A superfatted soap containing glycerin.
Myrrholin	Solution of myrrh in castor oil.
Naphtalol	β-naphtol benzoate (Betol).
Naphtopyrine	Compound of β-naphtol with antipyrine.
Naphtosalol	β-naphtol benzoate (Betol).
Nasrol	Symphorol.
Nico	Nickel carbonyl oxide.
Oleocreosote	Creosote oleate.
Oleoguaiacol	Guaiacol oleate.
Orexine	Phenyldihydroquinazoline.
Orthin	Ortho-hydrazine-para-oxybenzoic acid.
Oxychinaseptol	Oxychinoline ortho phenolsulphonate.
Parodyn	Antipyrine.
Pental	Trimethyl-ethylene.
Phenacetine	Para-acetphenetidine.
Phenazone	Antipyrine.
Phenine	Para-acetphenetidine.
Phenocoll	Amido-acet-para-phenetidine.
Phenolid	Mixture of acetanilide and sodium salicylate.
Phenolin	Mixture of cresols and soap.
Phenopyrine	Compound of carbolic acid and antipyrine.

TABLE V.—*Continued.*

Commercial Name.	Chemical Composition, or Description.
PHENOSALYL	Mixture of carbolic, salicylic, benzoic and lactic acid.
PHENYLON	Antipyrine.
PICROL	Di-iodo-resorcin-monosulphonic acid.
PICROPYRINE	Compound of picric acid and antipyrine.
PIXOL	Mixture of wood-tar and soap.
PYOCTANIN, BLUE	Methyl-violet.
" YELLOW	Auramine.
PYRODIN	Acetylphenylhydrazine.
PYROGALLOPYRINE	Compound of pyrogallol and antipyrine.
QUINALGENE	Synonym for Analgene.
RESORBIN	Ointment base consisting of almond oil, wax, gelatine, soap and water.
RESORCYLALGIN	Compound of resorcin and antipyrine.
RHODALLIN	Allylsulphocyanate (Thiosinamine).
RHODINAL	Paramidophenol.
RIXOLIN	Mixture of petroleum and light camphor oil.
SACCHARIN	Ortho-sulphamine-benzoic acid anhydride.
SALACETOL	Acetol salicylate
SALBROMALID	Antineurine.
SALINAPHTOL	β-naphtol salicylate (Betol).
SALIPHEN	Salicyl-phenetidin.
SALIPYRINE	Antipyrine salicylate
SALOL	Phenol salicylate.
SALOPHEN	Acetyl-amido-phenol salicylate.
SALOCOLL	Phenocoll salicylate.
SALUMIN	Aluminium salicylate.
SANATOL	Crude cresol-sulphonic acids.
SANGUINAL	A blood preparation.
SAPOCARBOL	Mixture of cresols and soap.
SAPROL	Mixture of cresols and hydrocarbons.
SEDATIN	Antipyrine.
"	Paravaleryamidophenetol.
SOLUTOL	Solution of cresols in sodium cresolate.
SOLVEOL	Solution of cresols in sodium cresotate.
SOMATOSE	Albumose preparation.
SOMNAL	Solution of chloral hydrate and urethane in alcohol.
SOZAL	Aluminium salt of para-phenol-sulphonic acid.
SOZOIODOLIC ACID	Di-iodo-para-phenol-sulphonic acid salts.
SOZOLIC ACID	Ortho-phenol-sulphonic acid.
STYRACOL	Guaiacol cinnamate.

TABLE V.—*Continued.*

Commercial Name.	Chemical Composition, or Description.
Styron	Cinnamyl alcohol.
Sucrol	Para-phenetol-carbamide (Dulcin).
Sulphaminol	Thio-oxy-diphenylamine.
Sulphonal	Di-ethylsulphone-dimethyl-methane.
Symphorol L	Lithium caffeine-sulphonate.
" N	Sodium caffeine-sulphonate.
" S	Lithium caffeine-sulphonate.
Tannal	Aluminium tannate.
Tannigen	Diacetyl-tannin.
Tetronal	Di-ethylsulphone-di-ethyl-methane.
Thermine	Tetrahydro-β-naphtylamine.
Thilanin	Sulphurated lanoline.
Thioform	Bismuth dithiosalicylate.
Thiol	Ammoninm salt of thiol-sulphonic acid.
Thiolinic acid	Sulphurated and sulphonated linseed oil.
Thiosapol	Soap containing sulphur in a state of chemical combination.
Thiuret	Oxydation product of phenyl-dithiobiurets.
Thymacetine	Ethoxy-aceto-amidothymol.
Thymotol	Dithymol-di-iodide (aristol).
Tolyl-hypnal	Compound of chloral hydrate with tolypyrine.
Tolypyrine	Para-tolyl dimethyl-pyrazolon.
Tolysal	Tolypyrine salicylate.
Tonquinol	Trinitro-iso butyl-toluene.
Trefusia	A natural iron albuminate.
Trikresol	Purified natural mixture of the three cresols.
Trinitrin	Nitroglycerin.
Trional	Di-ethylsulphone-methyl-ethyl-methane.
Tumenol	Sulphonated preparation of bitumenous oil.
Tussol	Antipyrine phenylglycolate.
Uralin	Chloral-urethane.
Uricedin	Mixture of sodium sulphate, chloride and citrate and lithium citrate.
Uropherin	Theobromine-lithium—lithium salicylate.
Vasogene	Mineral oil emulsified with water.
Vitalin	Solution of borax in glycerin.

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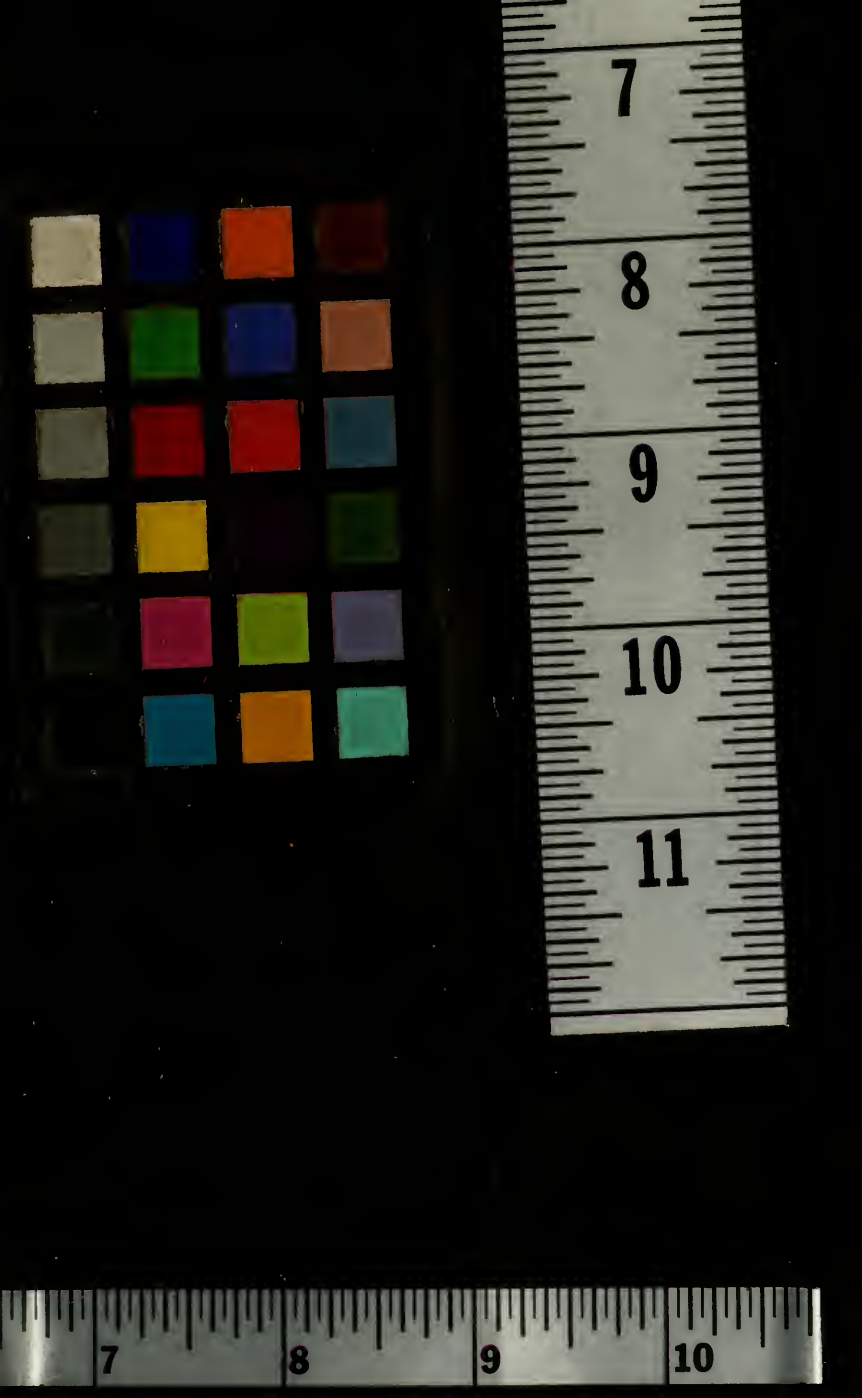
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